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RELATIONSHIP OF THE RHEUMATIC PROCESS TO THE DEVELOPMENT OF ALTERATIONS IN TISSUES

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I. CHARACTER OF TISSUE CHANGES ASSOCIATED WITH ACTIVITY OF THE RHEUMATIC PROCESS

In 1904 Aschoff [1] emphasized the association of the myocardial nodule with rheumatic fever. This marked the first recognition of histologic changes specific for rheumatic disease. During recent years the conception of the anatomic distribution of rheumatic lesions has been explained largely through the careful histologic studies of the pathologists. Vascular structures other than the cardiac muscle and valves have been found to be involved by the rheumatic process. Lesions specific in their histologic appearance have been described in the aorta by Klotz,[2] in the auricles by MacCallum,[3] in the blood vessels, aorta and auricles by Pappenheimer and VonGlahn [4] and in many other organs by Graff,[5] Paul [6] and Shaw.[7] That these lesions are extremely widespread in rheumatic fever has been demonstrated by the recent observations of Klinge,[8] who in detailed histologic studies [9] has admirably defined the stages in the development of rheumatic lesions throughout many parts of the human body. These descriptions, from Aschoff [1] through Klinge,[9f] have placed emphasis on the histologic appearance and the cellular reaction of the lesions which are specific, so far as is known, for rheumatic fever. In the present study, another group of tissue changes is presented. They have no distinct histologic appearance. Nevertheless,

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1. Aschoff, L.: Verhandl. d. deutsch. path. Gesellsch. **7**:46, 1904.
2. Klotz, O.: Tr. A. Am. Physicians **27**:181, 1912
3. MacCallum, W. G.: Bull. Johns Hopkins Hosp. **35**:329, 1924.
4. VonGlahn, W. C., and Pappenheimer, A. M.: Am. J. Path. **2**:235, 1926; **3**:583, 1927.
5. Graff, S.: Deutsche med. Wchnschr. **56**:603, 1930.
6. Paul, J. R.: Medicine **7**:383, 1928.
7. Shaw, A. F. B.: Arch. Dis. Childhood **4**:155, 1929.
8. Klinge, F.: Virchows Arch. f. path. Anat. **278**:438, 1930; **279**:1, 1930.
9. Klinge, F.: (*a*) Math.-phys. Klasse **86**:201, 1931; (*b*) Virchows Arch. f. path. Anat. **281**:701, 1931; (*c*) **284**:646, 1932; (*d*) **286**:314, 1932; (*e*) **286**:333, 1932; (*f*) **286**:344, 1932.

they seem to be of rheumatic origin, not only because they develop simultaneously with specific lesions, but also because they occur at a time when the rheumatic process appears clinically to be at the height of its activity.

The present study has been made on a group of 320 patients who died with rheumatic disease, who were observed by me during life, and who, in most instances, were examined post mortem. Death was not the result of rheumatic fever in all cases. Some patients died of other disease entities; many from bacterial infection of the endocardium; others of vascular accidents; a few of cardiac thrombosis; many of progressive heart failure, and in a large group death occurred during activity of the rheumatic process.

CAUSES OF DEATH OF PATIENTS WITH RHEUMATIC FEVER

Death from Other Disease Entities.—In this series of 40 patients, there were 35 in the rheumatic state in whom death could be attributed to other conditions. In all of these patients, histologic evidences of rheumatic disease were present. Some of them gave a history of having had rheumatic manifestations; in others, the morbid process had been insidious, and frequently unsuspected. The observations on these patients indicate that persons may live in the rheumatic state to old age (1 patient was 80, and 5 were over 50), and that the disease may be so mild that its symptoms at no time appear above the clinical horizon. These findings emphasize the difficulty attached to an accurate diagnosis of activity of the rheumatic process and demonstrate how the disease may smoulder. That rheumatic disease may occur concomitantly with other chronic diseases, such as cancer, tuberculosis, syphilis and diabetes, is evident.

Death Due to Bacterial Endocarditis.—Among this group of 49 patients with a definite history or anatomic evidence of rheumatism, bacterial endocarditis was the factor responsible for the termination of life. This group demonstrates the difference between rheumatic carditis and bacterial infection of the heart. Although the early stages of nonhemolytic streptococcic bacterial endocarditis simulated a rheumatic attack in many instances, the final outcome was clearly distinct. In only 1 patient was cardiac decompensation prominent. Death resulted from infection by occlusion of an important artery, from embolic nephritis and uremia or from the wasting which comes with long-standing invasion of the blood stream. The histologic findings emphasize the specifically distinct structures of the lesions due to rheumatic disease and bacterial infection. In some instances, the two types of lesions existed side by side in the heart; in others, without a history of rheumatic phenomena over a course of many years and without any histologic evidence of recent rheumatic activity, bacterial endocarditis manifested itself shortly after the extraction of teeth or the tonsils. Clumps of

organisms then appeared engrafted on valves which had been scarred by the rheumatic process in previous years. The nature of the death of these patients and the anatomic observations in this group emphasize the absence of any relationship between the mechanism of bacterial infection of the endocardium and the process responsible for rheumatic carditis.

Death Resulting from Vascular Accidents.—Sudden death of patients with rheumatic heart disease is not uncommon. Of this group, 38 patients died as a result of occlusion of an important artery. In most instances the patients were in early or middle adult life. Except in a few instances they had exhibited the physical and electrocardiographic signs of auricular fibrillation. At necropsy they presented the usual gross picture of long-standing heart disease with hypertrophy and dilatation, auricular thrombosis and an embolism in a pulmonary or a cerebral artery. Fresh rheumatic lesions were not conspicuous. Death resulted from an accident and not from rheumatic activity.

Death Due to Intracardiac Thrombosis.—Similar to the patients in the foregoing group, there were 8 patients who died suddenly as the result of large intracardiac antemortem thrombosis of a chamber of the heart. As among the patients just discussed, auricular fibrillation during life and the subsequent findings of long-standing heart disease with a tight mitral stenosis were conspicuous. Only traces of activity of the underlying disease remained.

Death Due to Long-Standing Rheumatic Heart Disease.—Perhaps the most common type of death among rheumatic patients is that resulting from long-standing cardiac decompensation with chronic passive congestion and eventual heart failure. In this series, 74 patients died from prolonged cardiac insufficiency. Their histories revealed the natural history of rheumatic disease; the chronicity of the process, probably beginning in early childhood and characterized by periods of quiescence and then frequent recrudescences following minor infections of the upper respiratory tract; the development of the physical signs of heart disease; the evolution of cardiac symptoms, terminating finally in inadequacy of the cardiac muscle to meet the demands made on it; then, the personal factor of unsuitable living conditions, economic difficulties, lack of facilities for prolonged rest, and—at last—repeated attacks of heart failure culminating in a period during which the patients experienced heart failure while at rest in bed. At necropsy, the results of chronic disease causing marked deformity of the heart were striking. While in most instances fresh rheumatic lesions were also present, it was the older lesions which constituted the striking part of the picture.

Death During an Acute Rheumatic Attack.—Of the 320 patients, more than 100 died in the course of active rheumatism. The organs of

these patients have been studied to determine the character of the changes in the tissues in relation to the activity of the disease process. In most instances death occurred after the patient had survived one or more cycles of the rheumatic attack. An illustrative example is presented.

CASE 1.—E. B., a girl, aged 9 years, was known to be rheumatic. She had an attack of carditis in the winter of 1931. During the spring months the disease was progressive. In June she experienced mild pains in the joints, and was found

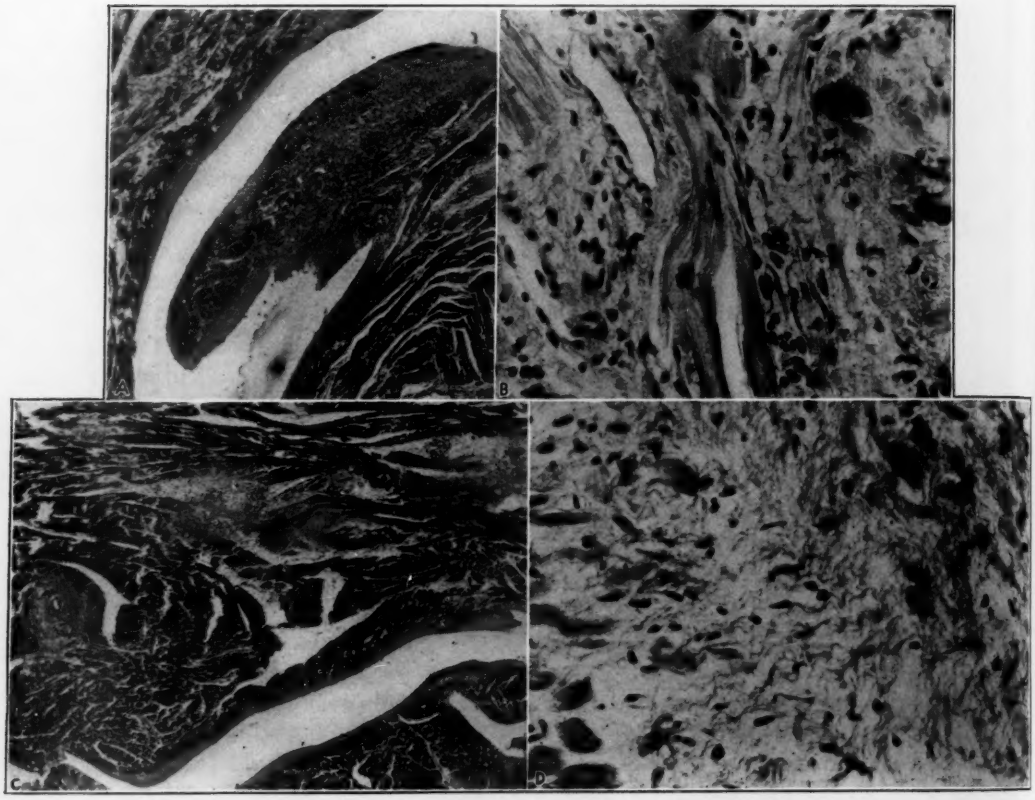

Fig. 1 (case 1).—Sections of the myocardium. *A* shows the widespread damage in a columna carneae. *B* is a highly magnified field of the columna carneae seen in *A*, and shows the complete destruction of myocardial bundles with replacement by cellular accumulations. *C* shows the large number of Aschoff bodies in a section of the left ventricle. *D* is a highly magnified field near an Aschoff body in the center of *C*, and shows the fragmentation of muscle fibers about the periphery of the Aschoff reaction.

to have a leukocytosis of 18,900 and a prolonged conduction time in the electrocardiogram, with a P R interval of 0.36 second. Although the body temperature was normal, the findings suggested marked activity of the rheumatic process. Two weeks after the onset of this cycle, the patient had a sudden attack of excruciating abdominal pain and died within a few hours.

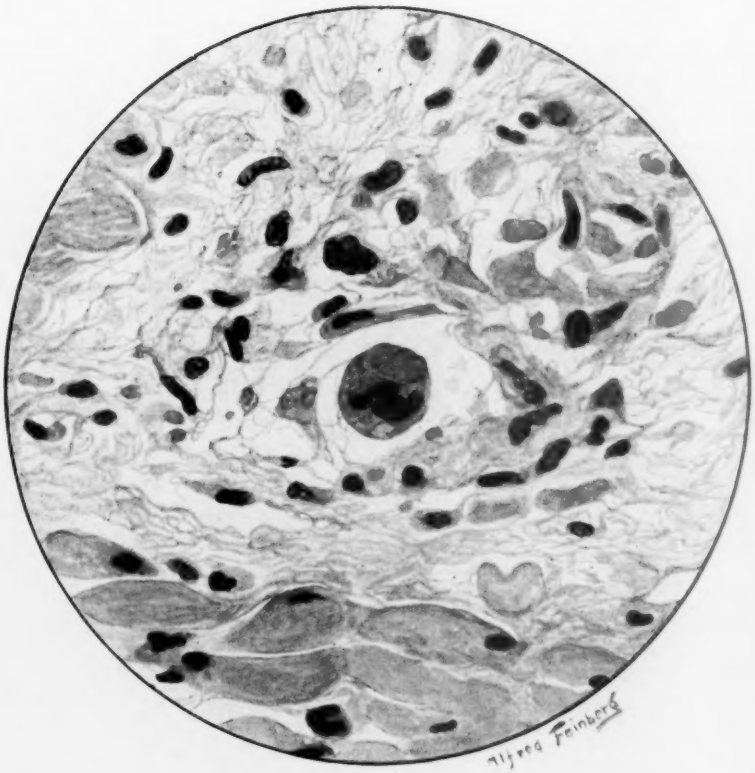

Fig. 2 (case 1).—This drawing was made from a highly magnified view of an Aschoff body in the left ventricle. The section had been stained with hematoxylin and eosin. Many fragments of collagen are seen in the Aschoff body, and the largest appears to be engulfed by the Aschoff cell.

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This patient, like a number of other children observed in the spring of 1931, survived the initial weeks of the rheumatic attacks, but died during a cycle of disease four months after activation of the process. The autopsy, performed by Dr. Beryl Paige at the Babies' Hospital, is summarized in the appendix.

The lesions found at autopsy may be grouped in two classes: First, changes having the specific character generally ascribed to rheumatic disease, and second, other lesions of a hemorrhagic character which did not present the generally accepted features of a rheumatic lesion. The former group included both changes of long standing, such as scarring of the myocardium, thickening of the cardiac valves and adherent pericardium, and fresh lesions, such as typical valvulitis, auriculitis and aortitis. Aschoff bodies were found in great numbers in the myocardium, especially along the course of blood vessels, where they appeared in closely packed clusters. In certain regions the formation of Aschoff bodies and the cellular infiltration were so widespread that the myocardial bundles were disrupted by them. In other sections, the cardiac fibers approximating the Aschoff bodies were swollen, frayed or completely destroyed. In many areas, particularly in some of the columnae carneae, the normal muscle cell structures were entirely absent and were replaced by débris and a variety of wandering cells. Although the necrosis of the collagen was intense, no micro-organisms were found. Aschoff cells were present in unusual quantity, both in typical Aschoff body formations and in collections of closely packed groups, but always in the proximity of necrotic collagen. In one instance, the Aschoff cell gave the appearance of phagocytosing a fragment of collagen. These were specific lesions. They suggested that damage had been taking place over a period of time, and that the histologic changes represented perhaps the beginning of repair.

In addition to these changes, which are generally recognized as rheumatic, another group of changes appeared to be of recent origin, and lacked the specific features of the rheumatic lesion. When the peritoneal cavity was opened, it presented the picture of purpura. Beneath the serosa of the mesentery and parietal peritoneum were innumerable hemorrhages, varying from 5 mm. to 6 cm. in diameter. A similar condition was found in the thoracic cavity. When the pericardium was incised, there were subserous hemorrhages varying from less than 1 mm. to 17 mm. in diameter. The microscopic observations likewise demonstrated extreme vasodilatation in many organs. The lungs contained areas of consolidation, characterized by marked capillary dilatation and by hemorrhagic edema of the alveoli and septums. Similar hemorrhagic lesions were observed in the ovaries, suprarenal glands, spleen and kidneys. The fresh appearance of these changes indicated that they had developed only a short time before death.

The chronicity of the rheumatic process and the cyclic character of the attack have been emphasized by many physicians. Corresponding to their descriptions, the majority of patients in my group experienced prolonged illness with many vicissitudes. When death occurred, it was preceded, in most instances, by months of active rheumatism, and a large number of specific lesions were found in the hearts of these patients. However, there were other patients in this group in whom rheumatic

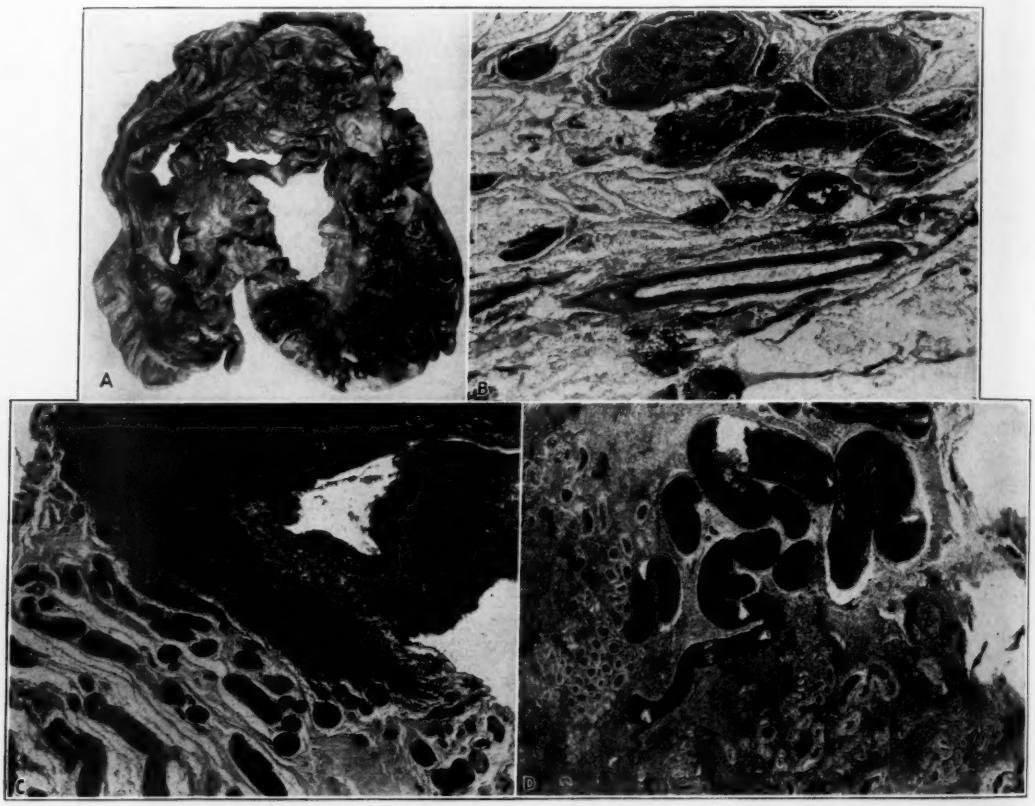

Fig. 3 (case 1).—Hemorrhagic lesions. *A* is a picture of the ecchymotic large bowel. *B* shows the microscopic appearance of the pinpoint hemorrhages in the mesentery near the cecum. *C* and *D* show extreme dilatation of the blood vessels and hemorrhage into the pericardium and ovary.

attacks developed which were rapidly fatal. In the tissues of these patients lesions without distinct histologic appearance were conspicuous.

The patient in the second case, who was nearly the same age as the one in the first case, died ten days after the onset of a rheumatic attack.

CASE 2.—J. N., a girl, aged 8 years, two weeks before admission contracted a sore throat and had fever. Twenty-four hours before admission she complained

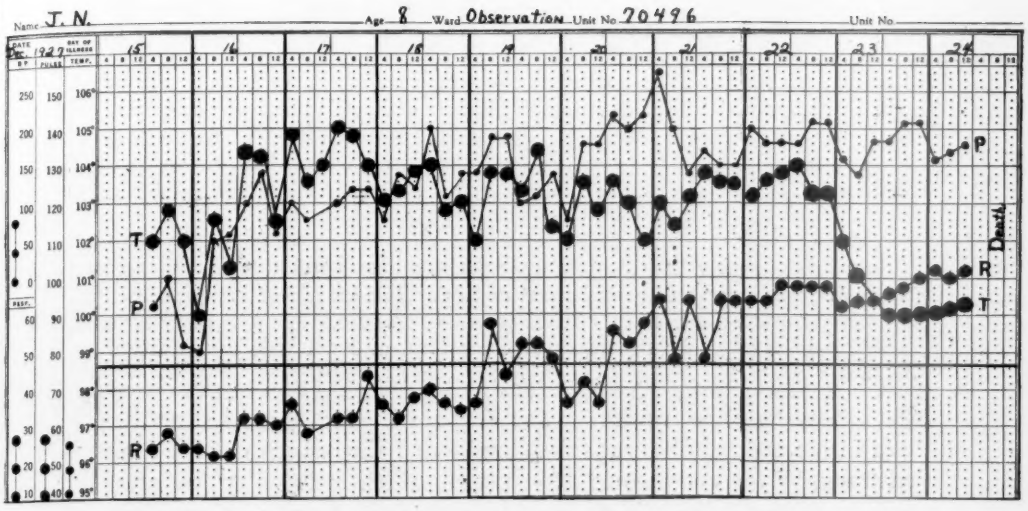

Fig. 4 (case 2).—The clinical course of a rheumatic attack, with the temperature (*T*), pulse (*P*) and respiration (*R*) from the onset of the symptoms until death on the tenth day of the illness.

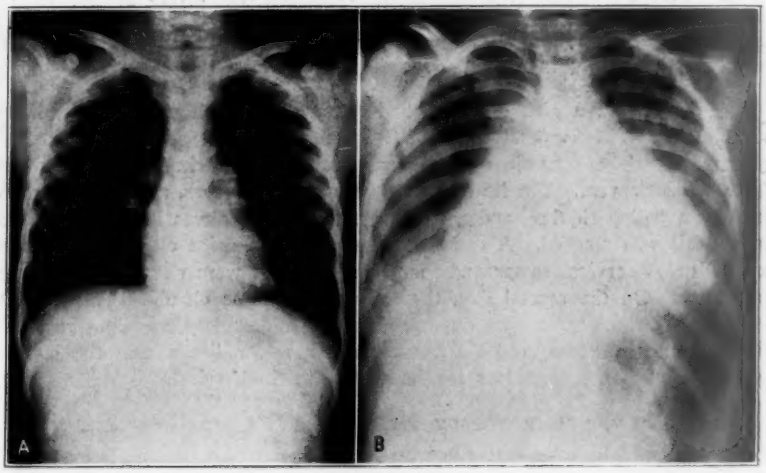

Fig. 5 (case 2).—X-ray pictures showing the rapid change in the size of the shadow of the heart. *A* was taken on the first day of the attack, when the heart was normal in size. *B* was taken on the third day of the attack, when the heart appeared to have dilated while the patient was at rest in bed.

of pain in both inguinal regions. Physical examination revealed a pale child, not uncomfortable and in no apparent distress. The tonsils were large and inflamed, and the cervical nodes were enlarged. A systolic murmur was heard at the apex of the heart. She had mild leukocytosis and signs suggestive of a small area of consolidation in the lung. Because of this an x-ray picture of the chest was taken; it showed nothing abnormal. Twenty-four hours after admission the temperature rose; the patient complained of pain in the abdomen, and she vomited. Then a pericardial friction rub became audible. Another x-ray picture of the chest, taken on the third day, showed that the cardiac shadow had become enormously enlarged, and suggested a pericardial effusion. Within a few hours the child was gravely ill. Signs of consolidation appeared at the bases of both lungs. Dyspnea and orthopnea became marked. Paracentesis of the pericardial sac was performed; only 10 cc. of clear fluid was obtained. The pulmonary signs shifted from day to day; the leukocytosis remained at 30,000, and the pulse was extremely rapid. She died quite suddenly ten days after admission.

The autopsy, performed by Dr. William C. VonGlahn, is summarized in the appendix. That this illness was a rheumatic attack is demonstrated by the microscopic observations, which included typical acute endocarditis and auriculitis. In addition to these specific lesions, there were hemorrhagic changes in the lungs which lacked the specific features of rheumatic lesions. In contrast to the changes in the patient in case 1, who died during the fourth month of an attack, there were few Aschoff bodies, and the detectable damage to the myocardium was limited to swelling and fragmentation of the collagen.

In another patient who was known to be rheumatic a recrudescence of the disease developed eighteen days following an infection of the upper respiratory tract, and she died on the seventh day of the attack. Her clinical history is as follows.

CASE 3.—M. G., a girl, aged 19, had rheumatism, with polyarthritis of two days' duration. The temperature was 104 F.; the pulse rate, 116, and the respiratory rate, 20. The sensorium was clear. Pains in the chest and joints were definite but not severe. The heart was not enlarged; however, the rate was rapid; there was a gallop rhythm, and a rough systolic murmur was heard at the apex. Leukocytosis was marked. A catheterized specimen of urine contained a few red blood cells. A cervical smear and four blood cultures were negative in a variety of mediums. On the second day, the sensorium became cloudy. This was followed by mania. A subconjunctival hemorrhage appeared in the right eye. The patient became comatose, and the temperature rose steadily during the last two days of life. Death occurred on the fourth day in the hospital.

The autopsy, performed by Dr. Homer Kesten, is summarized in the appendix. The lesions may be grouped in two classes: first, fresh lesions of typical specific character in the mitral valve, aorta and coronary arteries; second, widespread hemorrhagic changes in the retroperitoneal wall, over the sigmoid, in the mesentery, about the pelvic organs, throughout the thoracic cavity, in the substance of the tricuspid valve, at the base of the pulmonary valve, in the ventricular endocardium

and along the free margins of the mitral valve. These changes, present throughout the body, were most striking in the white matter of the brain.

This patient died at the height of a rheumatic attack. There was no history of bleeding or idiosyncrasy to drugs; there was no evidence of sepsis during the illness. Although she had a history of long-standing pelvic infection and contracted terminal bronchitis during the period of coma, repeated blood cultures remained sterile. At autopsy the observations of acute typical rheumatic lesions in the endocardium, aorta and arteries confirmed the clinical diagnosis. In addition, there were generalized capillary dilatation and hemorrhage without detectable lesions

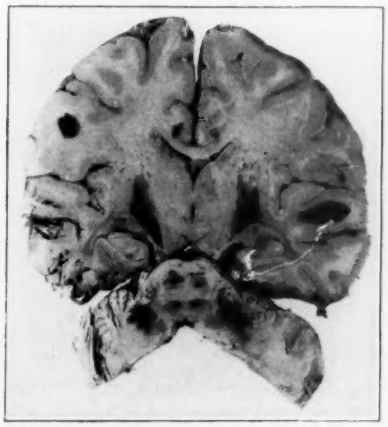

Fig. 6 (case 3).—Gross appearance of a transverse section of the brain, showing large areas of extravasated blood and innumerable punctate hemorrhages in the white matter, but rarely in the gray matter.

in the adjacent blood vessels. As in case 2, only a few Aschoff bodies were found, and there was swelling of the collagen in the myocardium.

The patients in cases 2 and 3 died during the first cycle of a rheumatic recrudescence. The patient in case 4 died one week after extraction of a tooth, on the fifth day of a rheumatic attack.

CASE 4.—F. C., a youth, aged 19, had enjoyed excellent health. Following the extraction of a tooth one week before admission, he bled profusely and then noticed swelling of his feet and hands, with soreness of his joints. The next day the urine became bright red, and pain developed under the sternum. Three days later physical examination revealed an acutely ill, pale boy, markedly dyspneic, orthopneic and cyanosed, with purulent exudate in his mouth. The chest was dull to percussion, both anteriorly and posteriorly, and was filled with bubbling râles; the heart was tremendously enlarged and overactive. The liver was enlarged to the umbilicus. There were marked secondary anemia and leukocytosis. The

urea content of the blood was 1.3 Gm. per liter. The urine contained casts and red and white blood cells. Blood cultures were sterile. The pulse became weak. A pericardial friction rub was heard. The patient died during the first day in the hospital.

The autopsy, performed by Dr. William C. VonGlahn, is summarized in the appendix. That the attack was of a rheumatic nature is clearly brought out by the typical early specific lesions in the mitral valve and the endocardium of the left auricle. As in the 2 preceding cases, only a few Aschoff bodies were found; however, swelling of the endothelium was widespread. The striking changes consisted of dilated capillaries and extensive hemorrhage without detectable alteration in

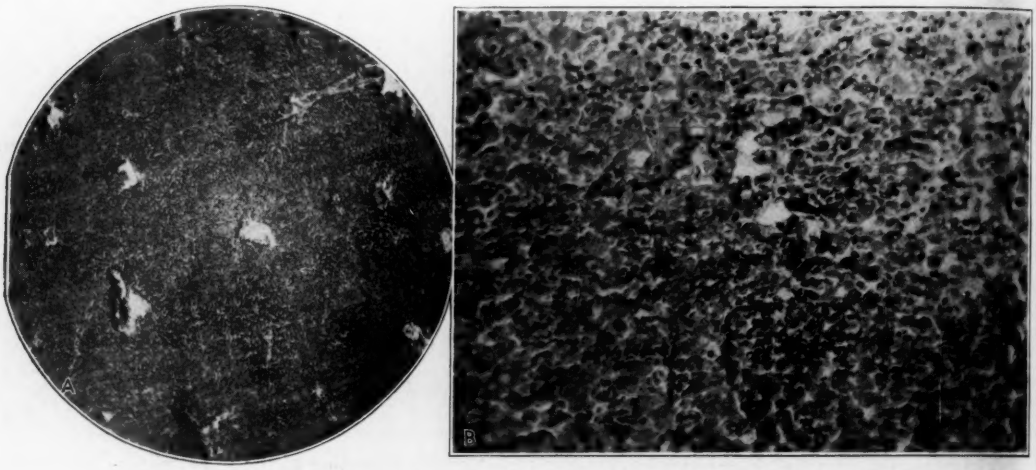

Fig. 7 (case 4).—Photomicrographs showing the alteration in the structure of the liver during the rheumatic attack. *A* shows the widespread central necrosis. *B* is a highly magnified view of one lobule, demonstrating the extensive hemorrhage about the efferent vein.

the structure of the adjacent blood vessels. Hemorrhagic lesions were conspicuous in the lungs and the liver, and were present in the pia over the brain.

As in the 3 preceding cases, the patient in case 5 died during the first cycle of a rheumatic attack.

CASE 5.—L. N., a boy, aged 16, with mitral stenosis, was under observation from July, 1930, until his death in January, 1931. He had not experienced cardiac insufficiency or any symptoms referable to the heart. On December 5, he contracted severe tracheitis. Two weeks later, while resting at home, he contracted bronchitis. This was accompanied by a return of rheumatic symptoms and tachycardia. Suddenly, edema of the face, oliguria and gross hematuria appeared in rapid succession. Vomiting and epistaxis reappeared and became distressing.

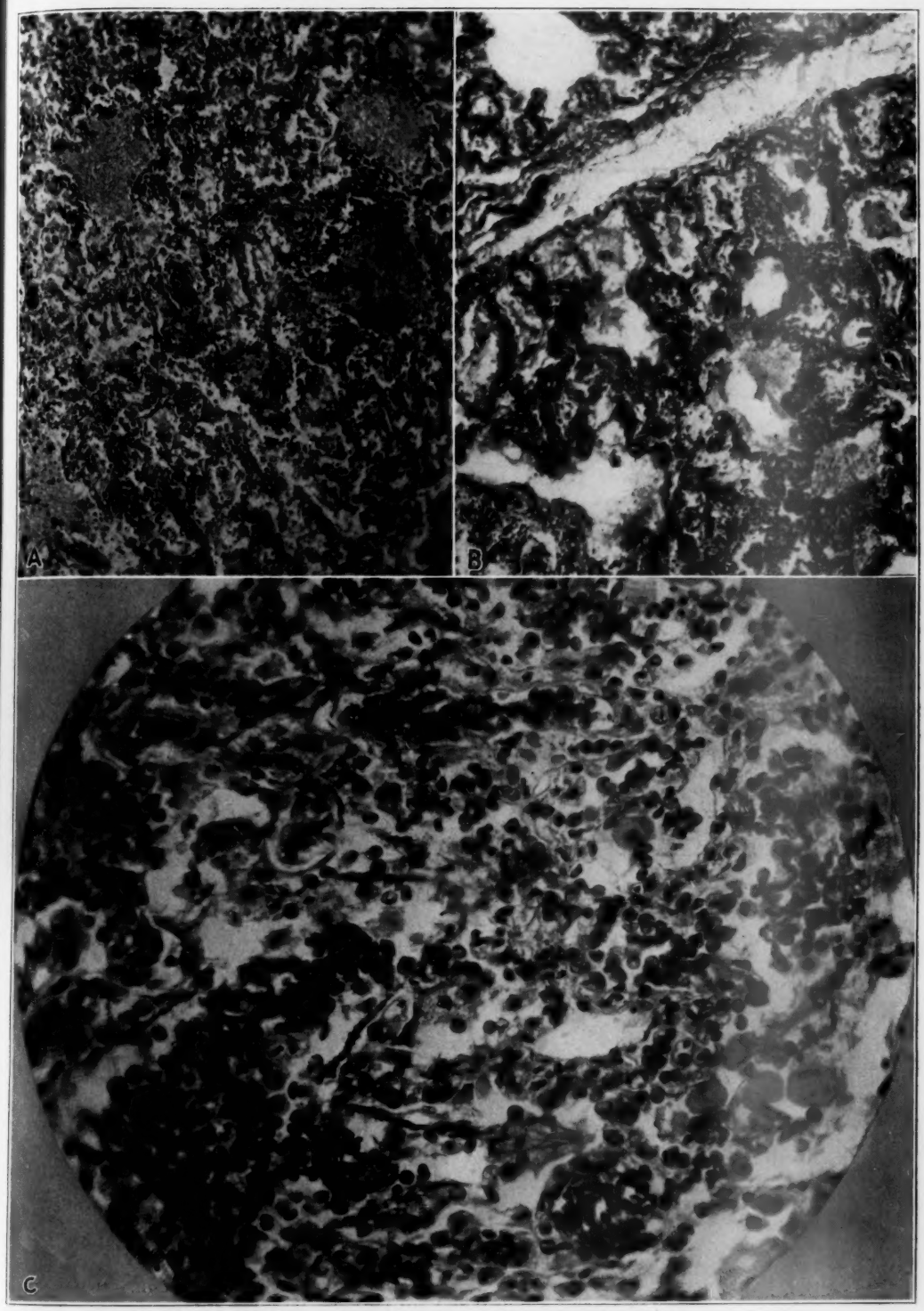

Fig. 8 (case 4).—Alterations in the structure of the lung during the rheumatic attack. *A* is a low power magnification of the consolidated lung. *B* is a highly magnified view of another area of the lung, and shows a hyaline membrane adherent to the walls of the alveolar sacs. *C* is an oil immersion view of *A*, showing capillary engorgement and alveoli filled with well preserved erythrocytes and collections of large pale-staining mononuclear cells.

He was taken to the Presbyterian Hospital, where he became uremic and died on the third day of acute nephritis.

The autopsy, performed by Dr. Homer Kesten, is summarized in the appendix. In addition to the infection of the bronchi, two groups of lesions were conspicuous. As in case 4, there was widespread hemorrhage, in the lungs, in the liver and scattered throughout many organs. In addition, there was an acute glomerulonephritis with extravasation of blood from the capillaries of the kidney. Although Aschoff bodies were not found, there were swelling and fragmentation of the collagen in the heart. The clinical diagnosis of a rheumatic attack was confirmed by the characteristic early specific lesions in the mitral valve and the auricular endocardium. The patient died of acute nephritis during a

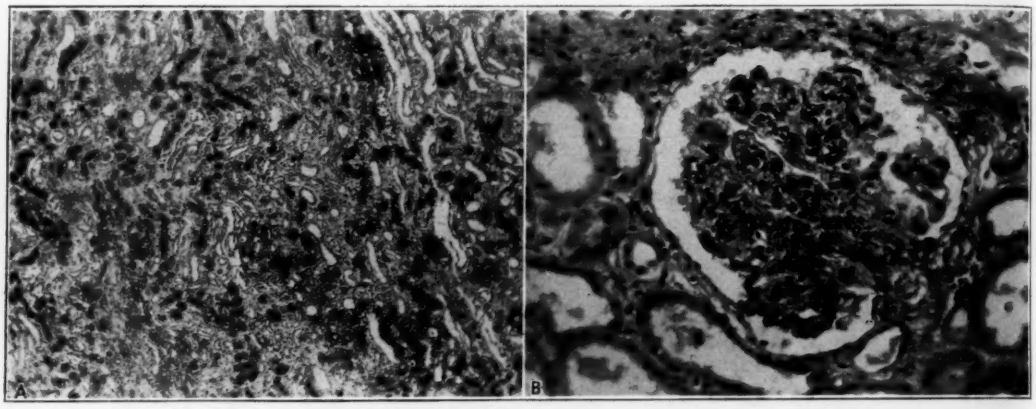

Fig. 9 (case 5).—Low and high power photomicrographs of sections of the kidney. In *A*, widespread hemorrhage is seen. *B* shows intracapillary changes of the glomerulus, with edema, hemorrhage and cellular proliferation.

rheumatic attack, an association that has been recorded by other observers.

These 5 patients were known to be rheumatic. Each contracted a respiratory infection, and each had a rheumatic attack. The patient in case 1 died after four months of active rheumatism; the others died during the first cycle of a recrudescence. That the disease process was rheumatic was established by the presence of fresh, typical, specific endocardial changes in each instance. In contrast to the changes in the patient in case 1, whose cardiac muscle contained many Aschoff bodies, the changes in the other patients consisted of swelling and fragmentation of the collagen and the accumulation of large cells about the blood vessels. In all the patients dying during marked activity of the rheumatic process, hemorrhagic lesions were widespread. The exact rela-

tionship of these lesions to the activity of the rheumatic process is especially well illustrated by case 6, in which death occurred shortly after the probable onset of the disease.

CASE 6.—R. R., a boy, aged 24 months, enjoyed excellent health until March, 1932, when he contracted scarlet fever. The attack was mild, and recovery was satisfactory. Two weeks later, however, infra-orbital edema was detected. This was followed by gross hematuria, a slight elevation in temperature and a rise in blood pressure to 120 systolic and 90 diastolic. After ten days, when his condition appeared to be improving, marked pallor developed. This was followed a few days later by purpura over both lower extremities. At this time the application of a tourniquet on the arm was accompanied by the appearance of numerous petechial hemorrhages below the tourniquet. Two days later, at the end of the fourth week, the patient suddenly became dyspneic and was admitted to the hospital. Physical examination revealed a desperately ill baby with an alabaster color, a temperature of 102 F., a pulse rate of 160 and a respiratory rate of 60. The heart was markedly enlarged and overactive. Diffuse signs of congestion were present over the lungs. There was a leukocytosis of 30,000. The urine contained albumin, red blood cells and casts. During the three days in the hospital, the liver became enlarged, and the temperature remained elevated. Dyspnea and extreme pallor persisted until death seventy-two hours after the onset of the cardiac symptoms.

This baby, who had been free from illness since birth, died on the third day of an attack of carditis. The autopsy, performed by Dr. Beryl Paige at the Babies' Hospital, is summarized in the appendix. The microscopic observations which established the diagnosis of rheumatic fever consisted of characteristic early specific lesions in the auricular endocardium and in the columnae carneae. In addition, there were focal lesions in the arteries of the kidneys, the liver and other organs. These lesions were similar to the vascular lesions described by Pappenheimer and Von Glahn,[4] now considered of rheumatic origin. No Aschoff bodies were found in the cardiac muscle, but swelling of the endothelial cells and fragmentation of the collagen were striking. About the blood vessels there were accumulations of large wandering cells, suggestive of Aschoff cells. In addition, there were small scattered hemorrhages throughout many organs.

In summary, this patient died in the twenty-fourth month of life, five weeks after the first recognized hemolytic streptococcic infection, during the initial cycle of the disease. The changes included areas of edema and hemorrhage in many organs, specific inflammatory reactions in the endothelium of the heart and blood vessels and fragmentation of the collagen in the myocardium. The cardiac lesions were comparable to those described by Fahr [10] and Siegmund [11] following scarlet fever and interpreted by them as being similar to the early specific lesions of rheumatic disease.

10. Fahr, T.: Virchows Arch. f. path. Anat. **232**:134, 1921.
11. Siegmund, H.: Centralbl. f. allg. Path. u. path. Anat. **44**:314, 1928.

Patients rarely die at the onset of a rheumatic attack, and the opportunity to examine organs during this stage of the disease is unusual. Nevertheless, it has been possible in a few instances (cases 7, 8 and 9) to study tissues obtained during the first few hours of rheumatic symptoms.

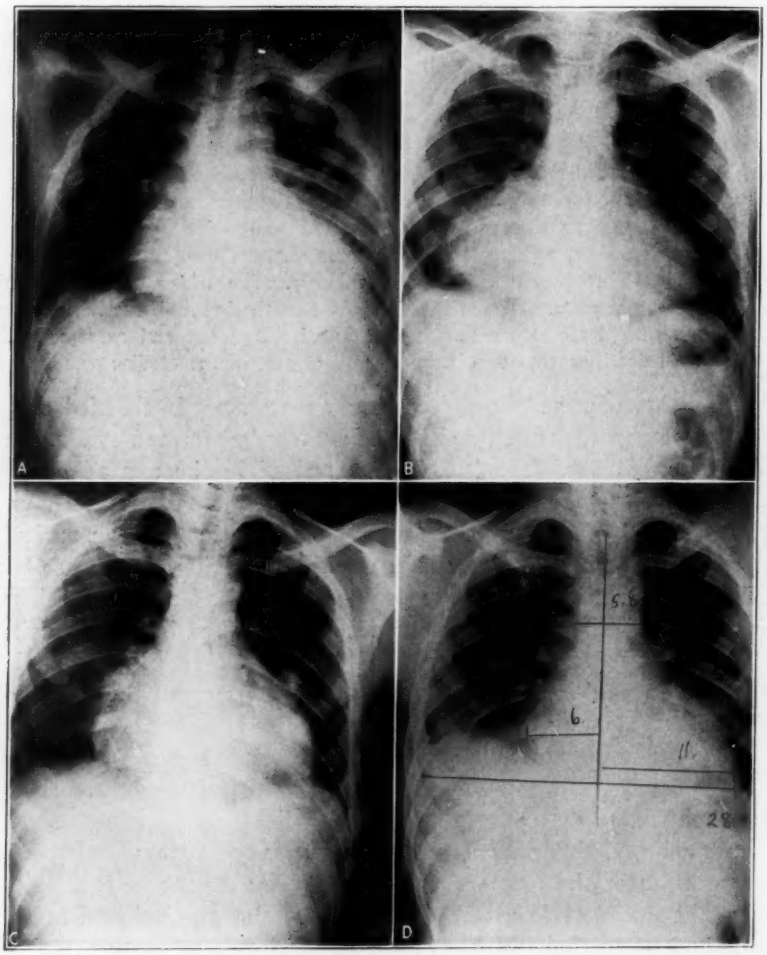

Fig. 10 (case 7).—X-ray pictures of the chest, demonstrating the changes in the thoracic viscera during the first two weeks of a rheumatic attack. In *A*, taken on May 23, 1931, there is consolidation of the upper lobe of the left lung. In *B*, taken on June 3, 1931, the lungs are normal, and there is a marked increase in the cardiac shadow, which on fluoroscopy was demonstrated to be due to a mediastinal effusion. In *C*, taken on June 8, 1931, the heart has reassumed its previous appearance. *D*, taken on Sept. 10, 1931, at a distance of 6 feet (about 2 meters), after three months of complete rest in bed, shows diffuse enlargement of the heart in all diameters.

CASE 7.—O. H., a colored boy, aged 18, experienced periumbilical pain, nausea and vomiting three weeks after a "sore throat" and "grip." The pain became intense and radiated to the urinary bladder. The physical signs suggested an abscess of the appendix. The white blood count was 34,000. Exploratory laparotomy was performed. The first week after operation pancarditis and mild polyarthritis developed. These changes were followed by transitory pulmonary solidification, pleurisy, a large mediastinal effusion, which disappeared in one week, hematuria, melena, a prolonged conduction time in the electrocardiogram and, finally, the physical signs of aortic insufficiency and mitral stenosis. The patient recovered after the picture characteristic of rheumatic heart disease had developed.

At the exploratory operation, the subcutaneous tissues, the muscles of the abdominal wall and the peritoneum were found infiltrated with edema. There was free fluid in the abdominal cavity. The large mass which had been palpated appeared to be composed of necrotic fat, which on microscopic study was found to

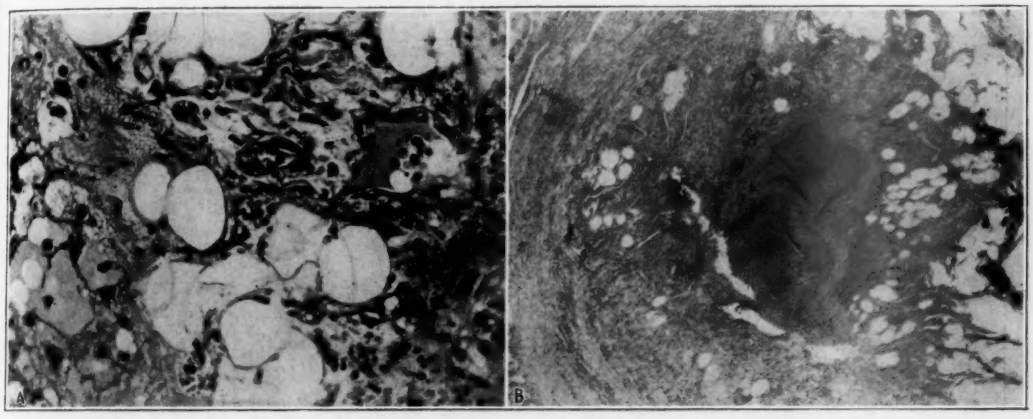

Fig. 11 (cases 7 and 8).—*A*, a highly magnified photomicrograph, was made from a section of a suprapubic mass in case 7. It shows capillary dilatation, marked edema, hemorrhage, necrosis of fat, cellular infiltration and deposition of fibrin. *B* shows extensive hemorrhage within the lumen of the appendix in case 8.

represent an acute inflammatory process with fibrinous exudate, extremely few inflammatory cells, proliferation of fibroblasts and capillaries and necrosis of fat. A summary of the observations is presented in the appendix.

In brief, this patient's rheumatic attack began with severe abdominal symptoms. A few hours later, exploratory operation revealed edema of the abdominal wall and peritoneum, subserous hemorrhage in the vermiform appendix and marked hemorrhagic necrosis of the provesical fat.

Similar changes were found in the vermiform appendix of another patient who underwent operation during the first few hours of a rheumatic attack.

CASE 8.—B. P., a man, aged 25, was attending a cinema when he was seized with sharp abdominal pain. Within two hours, the appendix was removed. The following day migratory polyarthritis and then typical rheumatic carditis developed. At operation the vermiform appendix had been found to be hemorrhagic. Histologic examination revealed a partially broken down blood clot in the lumen without evidence of inflammation. A summary of the observations is presented in the appendix.

In this patient the hemorrhages into the vermiform appendix were probably associated with active rheumatic disease. In other patients

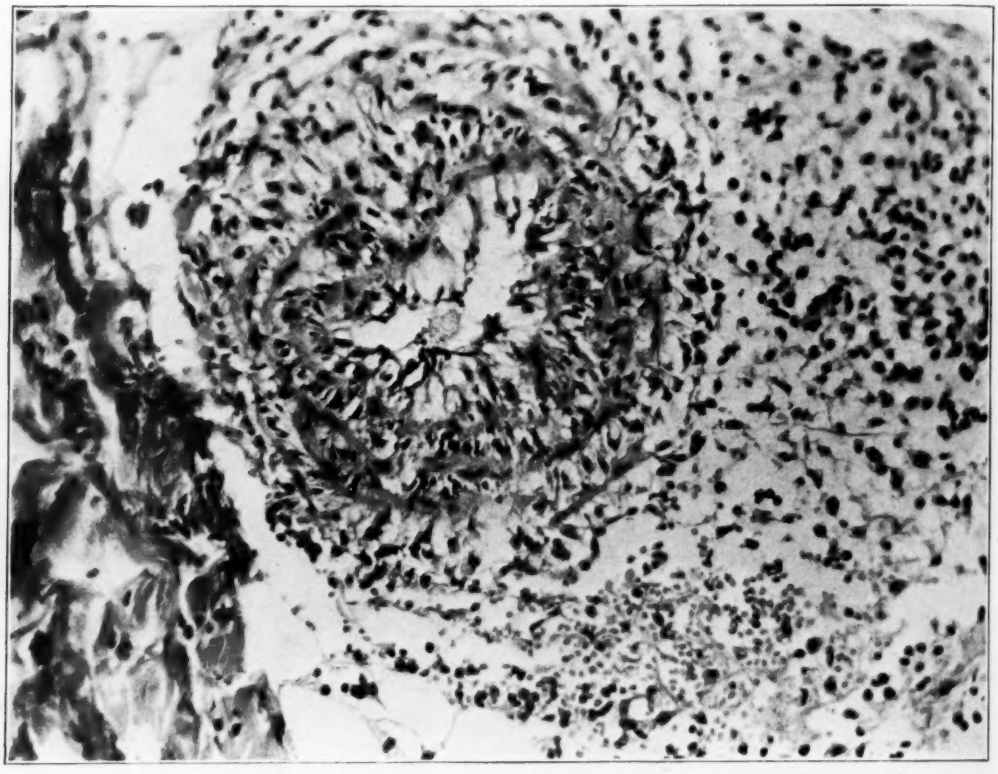

Fig. 12 (case 9).—This highly magnified photomicrograph represents a section of tissue involved by erythema nodosum. It shows striking swelling of the endothelial cells, which appear frayed out into the lumen; escape of erythrocytes through the wall of the vessel; swelling of collagen, and infiltration by wandering cells.

certain hemorrhagic lesions are not yet explained. An example of this is the intense hemorrhagic central necrosis of the liver [12] observed

12. Similar changes in the liver during acute attacks of rheumatism have been noted by many observers since the description of F. Ball (Du rheumatisme viscéral, Thèse de Paris, 1886).

during this study five times in association with fulminating rheumatic attacks. Whether these hepatic changes (case 4) are entirely a result of the activity of the rheumatic process or whether they are associated with acute congestion is not yet fully determined. In contrast to these obscure lesions of the abdominal viscera, the frank superficial hemorrhagic lesions have been correlated with other signs of activity of the rheumatic process. This is illustrated in a patient from whom a biopsy specimen was taken at the onset of erythema nodosum.

CASE 9.—In A. J., a young woman working in the hospital, erythema nodosum developed which was followed by polyarthritis. Biopsy of the skin was made during the first day of the cutaneous lesion.

The microscopic sections demonstrated a diffuse inflammatory lesion characterized by hemorrhage, perivascular round cell infiltration and deposits of fibrin. The striking changes were in the blood vessels; these showed a swelling of the endothelial cells, which appeared frayed out into the lumen. Throughout the connective tissue and the fat there were scattered foci of infiltration by polymorphonuclear leukocytes. There were also areas of swelling of the fixed tissue cells and an edematous appearance of the tissue itself. In one or two of these areas, multinucleated cells were seen. Microscopic studies of the blood vessels in this lesion showed the escape of erythrocytes through the wall of the vessel, causing hemorrhage into the surrounding tissues.

COMMENT

The tissues in the 9 cases presented were obtained during marked activity of the rheumatic process. The child in case 1 died during the fourth month of the attack. Aschoff bodies in many stages were numerous in the myocardium. The other patients died during the first fortnight of the attack. Although collections of large cells were detected about the blood vessels, there were few Aschoff bodies. Recognizable damage to the myocardium was limited to the swelling and fragmentation of the collagen. The diagnosis in each instance was established by the characteristic fresh specific lesion in the endocardium of the mitral valve and the left auricle. The conspicuous changes in these patients were lesions of a hemorrhagic character. They were not related to detectable alteration in the blood vessels, and did not present the generally accepted features of a rheumatic lesion. These hemorrhagic changes were closely associated with the clinical symptoms: acute abdominal pain in cases 1, 7 and 8, acute renal insufficiency in case 5, mania in case 3, cutaneous lesions in case 9 and asphyxia from hemorrhagic solidification of the lungs in case 4. Altogether, 5 of the 9 patients had a loose

hemorrhagic pulmonary consolidation.[13] The changes found in the lungs consisted in brief of subpleural and alveolar hemorrhage, with engorgement of the blood vessels; interstitial and alveolar edema; infiltration by wandering cells, resulting in a massive accumulation of large mononuclear cells in clusters, round cells, and rarely polymorphonuclears, deposition of a hyaline membrane along the walls of the alveolar sac, and the absence of detectable micro-organisms in the affected regions. These lesions—like those in the skin, brain, kidneys and thoracic and abdominal viscera—suggest alteration in vascular permeability with diapedesis and damage to the mesodermal tissues, accompanied in certain instances by inflammatory reaction.

In conclusion, the anatomic observations on these patients with acute rheumatism indicate that, in addition to the well recognized swelling of endothelium and fragmentation of collagen, diffuse hemorrhagic changes are characteristic of activity of the rheumatic process.

II. CHARACTER OF PHYSIOLOGIC CHANGES ASSOCIATED WITH ACTIVITY OF THE RHEUMATIC PROCESS

When it has been possible to study the tissues of patients during the first two weeks of a rheumatic attack, hemorrhagic lesions have been conspicuous. These lesions, so far as was determined, have appeared in most instances to be unassociated with demonstrable alteration in the structure of the blood vessels. They have occurred, however, with great frequency during the phase of marked rheumatic activity. The second part of these studies is presented to define the clinical relationship between the development of hemorrhagic lesions and the evolution of the rheumatic process.

The course of rheumatic fever is punctuated with a variety of bizarre clinical phenomena. Of these, the only recognizable lesion with specific histologic structure is the subcutaneous nodule. Nodules have been found in 15 per cent of my group of rheumatic subjects during the period of observation. However, they have in no instance been observed during the first two weeks of the rheumatic attack; in many patients they have been detected when the disease was subsiding; in some

13. During the progress of this study of the "rheumatic lung," a number of other observers described this manifestation of the disease. Among the 320 deaths on which this study is based, there were 45 instances of hemorrhagic pulmonary solidification. The clinical changes were comparable to those outlined by M. A. Rabinowitz (Rheumatic Pneumonia, J. A. M. A. **87**:142 [July 17] 1926); the anatomic changes, with one exception, were similar to the observations of A. E. Naish (Lancet **2**:10, 1928), Paul,[6] A. D. Fraser (Lancet **1**:70, 1930) and B. A. Gouley and J. Eiman (Am. J. M. Sc. **183**:359, 1932). Fraser described Aschoff's nodules in the interlobar septums; Gouley and Eiman have also observed these nodules. In my group of patients with rapidly fatal disease, pulmonary lesions with specific histologic structures have not yet been demonstrated.

they have developed even after the rheumatic process seemed inactive.[14] The time of appearance of the subcutaneous nodules in these patients has been between forty and seventy-two days following respiratory infection with the hemolytic streptococcus, that is, during the stage of recovery from the initial damage to the tissue. The sequential relationship of these nodules to other rheumatic lesions is illustrated in table 1.

TABLE 1.—*Clinical Stages in the Evolution of Rheumatic Fever and the Anatomic Observations in Rheumatic Subjects Dying of Acute, Rapidly Fatal Rheumatic Carditis, of Progressive Continuous Activity of the Rheumatic Process or of Vascular Accidents with a Mechanically Deformed Heart*

Period of Disease	Clinical Manifestations	Cause of Death	Anatomic Observations
Rheumatic subject in normal health	None	Another disease	Aschoff bodies may be found in the myocardium
Evolution of rheumatic process			
First phase	Brief infection of upper respiratory tract with hemolytic streptococcus		
Second phase	Symptom-free period of about two weeks		
Third phase	Rheumatic attack: fever, epistaxis, pallor, pain, diaphoresis, erythemas, urticaria, cephalalgia, edema, purpura, hematuria, pancarditis, polyarthritis, pleurisy, pulmonary solidification, polyserositis, chorea and other disturbances of the nervous system	Activity of the rheumatic process	Nonspecific lesions: edema of many tissues, engorgement of blood vessels, swelling of endothelium, swelling and fragmentation of collagen, hemorrhage, wandering cell infiltration, inflammation of pleura, pericardium or peritoneum. "Specific" histologic response: endocarditis, auriculitis, arteritis, perivascular collections of ? Aschoff cells in the myocardium
Subacute, continued activity and healing	Subcutaneous nodules, wasting, anemia, decreasing myocardial reserve	Progressive myocardial damage	Aschoff bodies and other "specific" lesions conspicuous
Heart disease, rheumatic process inactive	Symptoms of cardiorespiratory embarrassment	Heart failure due to mechanical changes or to vascular accident	Hypertrophy and dilatation of the heart, fibrosis and calcification of the valves, scarring of the myocardium, vascular embolus, thrombosis or chronic passive congestion, Aschoff bodies inconspicuous

In contrast to the late development of nodules on the tendon sheath, there is a group of rheumatic manifestations which appear at the onset of the disease and suggest functional changes of the blood vessels. In most instances these changes are mild, perhaps of a vasomotor nature, giving rise to pallor, angioneurotic edema, urticaria, iritis, laryngeal edema and transitory erythema marginatum. In some instances, how-

14. Findlay in Glasgow (Rheumatic Infection in Childhood, London, Edward Arnold & Co., 1931) has also observed the striking difference in the time of appearance of polyarthritis and subcutaneous nodules in rheumatic children.

ever, the changes are severe and seem to be associated with marked alteration in the permeability of walls of the vessels. This is suggested by the occurrence of epistaxis, purpuric erythemas and hemorrhages from the urinary tract, the respiratory tract and the intestinal tract in the absence of demonstrable changes in the blood. The relative frequency of these hemorrhages is illustrated by the incidence of 96 nosebleeds among 15 of 30 convalescent rheumatic children. During the same period of six months, among 200 acutely ill rheumatic patients, 4 experienced melena, 1 hemorrhagic edema of the larynx, 1 hemoptysis and 1 hematemesis. The blood findings were normal in all. Proctoscopic examination in a patient with melena revealed punctiform hemorrhagic areas in the lower bowel with active oozing of blood and without mucus or exudate. With the same suddenness that characterized the onset of the hemorrhage, it stopped in about ten days, and the mucosa of the bowel became normal. The changes in the patient with edema of the larynx were similar: dilated vessels with edema and oozing of the blood in the upper respiratory passages; the cessation was as abrupt as the onset. In brief, the clinical studies have suggested that during the rheumatic attack generalized damage to vascular structures occurs, and that one expression of this alteration in function is hemorrhage. In most instances the hemorrhage was slight and distributed in such a way that it was not readily measurable. However, since methods [15] are available for detecting small hemorrhages in the urinary tract, a study was made to determine the exact relationship between the escape of red blood cells from the blood vessels and the activity of the rheumatic process. The subjects included rheumatic patients with cardiac decompensation and those experiencing acute rheumatism without marked myocardial insufficiency.

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15. William Goldring (Am. J. M. Sc. **182**:105, 1931; J. Clin. Investigation **10**:345, 1931), using the Addis technic (Addis, T.: J. Clin. Investigation **2**:409, 1926), made observations on the urinary sediment count in infections. Following recovery from lobar pneumonia, in a few instances he noted changes suggesting acute focal nephritis. In patients with heart disease and chronic passive congestion, the urine contained the normal number of red blood cells. In the urine of 19 of 31 adults experiencing acute rheumatism not treated with salicylates, an abnormally large number of red blood cells was found. These instances of hematuria minima were not accompanied by the other findings of acute nephritis. J. Lyttle (J. Clin. Investigation **12**:95, 1933), in studying patients recovering from scarlet fever, observed that although urinary findings suggesting mild nephritis developed in only a few, all manifested a shower of red blood cells in the urine during the second or third week of convalescence. This was later found to be true also of patients recovering from other types of hemolytic streptococcic disease. Following the acute transient infection, this increase of red blood cells in the urine was present, but for only a few days.

In the cases of long-standing progressive heart disease, the urinary findings did not show striking changes and are not presented here.

When rheumatic subjects contract hemolytic streptococcic infections of the throat and are placed in bed for observation, the events which follow may vary a great deal. The majority of my patients manifested mild rheumatic symptoms about two weeks after recovery from pharyngitis; a smaller number had severe, frank attacks of acute rheumatism; an occasional patient experienced the clinical picture of acute nephritis in addition to polyarthritis and carditis. Examples of these three types of responses and the urinary changes will be detailed.

CASE 10.—P. W., a rheumatic youth, aged 18, was under observation for seven years. He had been symptom-free for three years when, on March 25, 1932, he contracted hemolytic streptococcic infection of the throat. He was admitted to the hospital where the local infection subsided on the second day. The temperature and leukocyte count returned to normal. On the tenth day, his temperature rose to 100 F., where it remained for seventy-two hours, with a rise in the leukocyte count from 8,000 to 11,000. This was followed by erythema marginatum symmetrically distributed over both arms, mild polyarthritis and a rapid recovery.

The results of a study of the sediment in the urine during this period is summarized in table 2.[15a]

TABLE 2.—*Results of Examination of Urine in Case 10*

Date	Time of Taking Specimen, Hours	Volume, Cc.	Specific Gravity	p_H	Protein		Casts	Red Blood Cells	Epithelial Cells
					Per Cent	Amount, Mg.			
3/28/32	12	500	1.015	6.1	0.004	18.00	83,333	150,000	650,000
4/ 1/32	12	465	1.016	6.0	0.004	16.74	15,500	232,500	139,500
4/ 6/32	12	430	1.005	6.3	0.004	15.48	25,889	1,075,000	?
4/11/32	12	485	1.015	6.3	0.007	34.92	26,944	630,500	388,000
4/13/32	12	450	1.022	6.0	0.004	16.20	40,000	900,000	450,000

From table 2 it is seen that on April 6, 1932, when malaise and a slight elevation in temperature with leukocytosis were present, there was a simultaneous slight rise in the red blood cell count of the urine. This rise was temporary and similar to that observed in nonrheumatic patients recovering from hemolytic streptococcic pharyngitis.

In contrast, in another patient a severe reaction developed, with intense rheumatism and striking urinary changes.

CASE 11.—P. N., a rheumatic girl, aged 10 years, attended school at the Pelham Home. She was admitted there in the fall of 1931 with mitral stenosis and a history of repeated rheumatic attacks. The last attack had occurred in June, 1931, and was characterized by polyarthritis, chorea and hematuria. At the Pelham Home signs of activity persisted during the fall months, but entirely disappeared during the winter. On March 14, the patient contracted hemolytic streptococcic

15a. The urinary determinations presented in this article were made by Carol Hazelton.

pharyngitis. Two weeks later a severe rheumatic attack with pancarditis developed. The course of intense activity persisted for two months. The results of a study of the sediment in the urine during this period are analyzed in table 3.

The patient in case 11, who had previously shown urinary changes, contracted marked hematuria on March 30, 1932, twelve days after infection. Forty-eight hours later she had fever, then polyarthritis and later signs of carditis. During this illness the number of erythrocytes in the urine increased. The course of hematuria minima ran parallel to the apparent activity of the rheumatic process. Its onset preceded the recognized manifestations of acute rheumatism by twenty-four hours.

TABLE 3.—*Results of Examination of Urine in Case 11*

Date	Time of Taking Specimen, Hours	Volume, Cc.	Specific Gravity	p_H	Protein		Casts	Red Blood Cells	Epithelial Cells
					Per Cent	Amount, Mg.			
12/28/31	12	305	1.026	6.2	0.007	21.96	0	21,960,000	5,307,000
1/ 4/32	12	270	1.030	6.1	0.007	19.44	0	46,805,000	30,155,000
1/11/32	12	370	1.018	5.6	0.007	26.64	61,667	22,755,000	12,580,000
1/18/32	12	345	1.020	5.6	0.007	24.84	0	17,767,500	13,800,000
1/25/32	12	340	1.017	6.1	0.004	12.24	0	18,700,000	7,650,000
2/ 3/32	12	530	1.010	6.2	0.004	19.08	0	1,749,000	7,155,000
2/11/32	12	285	1.020	5.8	0.007	20.16	12,666	3,762,000	2,280,000
3/ 9/32	12	235	1.022	6.2	0.007	16.72	0	15,862,000	11,515,000
3/16/32	12	260	1.028	6.1	0.004	9.36	0	6,630,000	5,694,000
3/23/32	12	435	1.013	5.7	0.004	15.66	0	22,337,500	14,094,000
3/30/32	12	475	1.019	6.3	0.007	34.20	0	70,775,000	16,150,000
4/ 6/32	12	295	1.020	5.6	0.007	21.24	0	23,600,000	3,392,500
4/13/32	12	285	1.016	5.5	0.007	2-.52	79,167	78,090,000	5,700,000
4/17/32	12	200	1.020	6.1	0.007	14.40	33,333	28,500,000	4,500,000
4/20/32	12	310	1.027	6.1	0.007	22.32	0	41,850,000	5,115,000
4/27/32	12	330	1.026	5.8	0.004	11.88	275,000	37,950,000	6,600,000
5/ 1/32	12	305	1.023	6.2	0.007	21.96	84,722	55,662,500	3,812,500
5/ 4/32	12	340	1.023	5.8	0.014	48.96	168,890	96,560,000	8,160,000
5/11/32	12	360	1.022	6.2	0.004	12.96	0	34,740,000	6,840,000
5/18/32	12	260	1.024	6.3	0.007	18.72	0	29,640,000	7,800,000
5/25/32	12	635	1.010	6.2	0.004	22.86	0	12,954,000	2,857,500
6/ 1/32	12	395	1.016	6.3	0.004	14.22	285,278	37,525,000	4,542,500
6/ 7/32	12	475	1.013	6.2	0.004	17.10	131,944	30,875,000	1,187,500
6/15/32	12	360	1.023	5.7	0.007	25.92	0	72,360,000	2,160,000
6/22/32	12	340	1.024	5.4	0.007	24.48	56,667	106,760,000	4,760,000

In case 2, the severe rheumatic attack was accompanied by high fever. Another patient, in whom acute, but less intense, rheumatism developed with only a slight elevation in temperature, experienced a more marked hematuria.

CASE 12.—H. R., a boy, aged 14, was observed for four years. In 1928 he had a severe rheumatic attack which resulted in marked cardiac damage. During the winter of 1932 an infant sister, following hemolytic streptococcic pharyngitis, contracted rheumatic fever with carditis. The patient experienced mild symptoms. On April 14, he contracted hemolytic streptococcic infection of the throat. The electrocardiogram was normal until ten days later, when the tracing showed striking changes, including a prolonged conduction time, with a P R interval of 0.23 second and an elevation of the S T interval, interpreted as indicating activity of the rheumatic process in the cardiac muscle. Another electrocardiogram was taken two days later, and the findings were confirmed. During the following weeks the patient had the signs characteristic of pancarditis.

The urinary determinations are presented in table 4.

In this patient electrocardiographic changes and hematuria minima developed ten days after recovery from hemolytic streptococcic infection of the throat. The hematuria began with the onset of activity of the rheumatic process and increased as the activity became more intense. The urinary findings of pyuria and cylindruria, during the fourth week suggested nephritis.

The rheumatic process was probably still active in cases 11 and 12 when recrudescences developed. In the next case, however, the clinical and laboratory observations indicated that the disease was quiescent

TABLE 4.—*Results of Examination of Urine in Case 12*

Date	Time of Taking Specimen, Hours	Volume, Cc.	Specific Gravity	p_H	Protein		Casts	Red Blood Cells	Epithelial Cells
					Per Cent	Amount, Mg.			
4/14/32	12	790	1.015	6.2	0.007	56.88	0	13,114,000	4,740,000
4/18/32	12	450	1.018	6.1	0.014	64.80	500,000	15,300,000	4,410,000
4/20/32	12	485	1.020	5.9	0.007	34.92	26,944	8,730,000	1,940,000
4/25/32	12	195	1.024	5.5	0.014	28.08	86,667	20,085,000	14,625,000
4/27/32	12	325	1.013	5.6	0.004	11.70	1,047,222	49,562,500	123,500,000
5/ 1/32	12	515	1.023	6.2	0.014	74.16	801,111	208,060,000	96,047,500
5/ 5/32	12	480	1.026	5.6	0.007	34.56	266,667	369,600,000	40,800,000
5/ 9/32	12	760	1.024	5.7	0.014	109.44	422,222	1,292,000,000	41,800,000
5/12/32	12	770	1.025	5.8	0.014	110,88	0	777,700,000	46,200,000
5/13/32	12	1,025	1.019	6.0	0.007	73.75	0	451,000,000	46,125,000
5/18/32	12	790	1.021	6.1	0.007	56.18	219,444	171,825,000	9,085,000
5/20/32	12	820	1.020	5.8	0.007	59.04	136,667	133,250,000	7,380,000
5/20/32	12	580	1.020	5.9	0.011	62.64	322,222	99,470,000	5,800,000
5/25/32	12	580	1.020	5.9	0.011	62.64	322,222	99,470,000	5,800,000
5/25/32	12	890	1.004	6.3	0.004	32.04	89,000	17,355,000	1,335,000
5/27/32	12	590	1.016	5.5	0.011	64.22	27,041,667	110,625,000	13,275,000
5/30/32	12	740	1.017	5.5	0.011	79.92	411,111	48,100,000	28,120,000
6/ 3/32	12	170	1.027	5.5	0.004	6.12	94,444	24,225,000	2,125,000
6/ 6/32	12	290	1.030	5.5	0.004	10.44	319,000	33,930,000	3,306,000
6/ 8/32	12	245	1.030	5.5	0.004	8.82	748,611	45,692,500	5,512,500
6/10/32	12	295	1.031	5.5	0.004	10.62	295,000	25,075,000	2,950,000
6/13/32	12	200	1.036	5.6	0.011	21.60	1,266,000	15,180,000	2,880,000
6/17/32	12	525	1.021	6.3	0.007	37.80	151,666	10,500,000	840,000
6/20/32	12	405	1.021	6.2	0.007	29.16	135,000	5,913,000	648,000
6/22/32	12	540	1.024	6.0	0.007	38.88	54,000	31,266,000	1,620,000
6/29/32	12	375	1.018	6.0	0.004	13.50	62,500	11,250,000	5,625,000
7/ 1/32	12	370	1.026	5.9	0.007	26.64	411,111	40,330,000	3,700,000

over a period of two years previous to the onset of an acute infection of the upper respiratory tract.

CASE 13.—N. S., a youth, aged 19, had been in a ward of the Presbyterian Hospital in 1929 with a typical attack of rheumatic fever. For over two years he remained symptom-free. The signs of mitral stenosis persisted; however, the clinical and laboratory observations were normal. Two cultures of the flora from the throat were made each month, and no pathogenic organisms were found. On December 15, the patient contracted mild pharyngitis, and examination of the flora of the throat demonstrated in almost pure culture the hemolytic streptococcus, which had been absent for more than two years. Within three days the pharyngitis subsided; the fever and leukocytosis disappeared, and the hemolytic streptococcus was no longer recovered from the surface of the pharynx. On December 29, although the patient remained symptom-free, the leukocyte count rose to 15,900, and the electrocardiogram showed premature ventricular contractions. Then the pulse rate rose from 80 to 118, and finally on December 31, sixteen days after the onset of infection, the patient became ill. The picture characteristic of rheumatic

fever made its appearance during the first week of January, with a temperature of 102 F., pains in the muscles, mild migrating polyarthritis, and leukocytosis. On January 8, salicylate therapy was begun, and the fever and pain subsided promptly.

The urinary determinations are presented in table 5.

This rheumatic subject apparently remained free from hemolytic streptococcic infection and rheumatic manifestations for three years. Then he contracted pharyngitis with Streptococcus haemolyticus. During the stage of infection, there was a slight increase in the excretion of red cells in the urine. In the second stage, a quiescent interval of ten days, the urinary observations were normal. On the seventh day of the rheumatic attack, there was a striking rise in the urinary excretion of erythrocytes. As for the previous patients, salicylate therapy was not instituted until after the first week of rheumatic fever.

TABLE 5.—*Results of Examination of Urine in Case 13*

Date	Time	Volume, Cc.	Specific Gravity	p_H	Protein		Casts	Red Blood Cells	Epithelial Cells
					Per Cent	Amount, Mg.			
12/18/32	4 p.m. - 7 p.m.	970	1.031	6.1	0.007	55.87	0	2,172,800	4,500,800
12/19/32	12 hr. specimen	300	1.020	6.0	0.007	21.60	8,333	750,000	1,425,000
12/29/32	12 hr. specimen	370	1.027	6.1	0.007	26.64	32,889	740,000	2,035,000
1/ 4/33	12 hr. specimen	600	1.016	6.2	0.011	64.80	0	900,000	780,000
1/ 5/33	7 p.m. - 7 a.m.	1,000	1.007	6.2	0.018	180.00	222,222	800,000	500,000
1/ 6/33	12 hr. specimen	630	1.014	6.3	0.014	90.72	0	2,079,000	1,134,000
1/ 7/33	12 hr. specimen	500	1.008	6.0	0.014	72.00	222,222	145,000,000	3,250,000
1/ 9/33	12 hr. specimen	455	1.011	6.1	0.014	65.52	75,833	320,775,000	5,687,500
1/10/33	12 hr. specimen	450	1.022	6.0	0.014	64.80	0	375,300,000	5,625,000
1/11/33	12 hr. specimen	390	1.013	6.2	0.004	14.04	39,000	5,031,000	1,755,000
1/12/33	12 hr. specimen	500	1.022	6.2	0.004	18.00	88,889	15,300,000	2,500,000
1/13/33	12 hr. specimen	495	1.024	6.2	0.007	35.64	165,000	9,900,000	2,475,000
1/14/33	12 hr. specimen	480	1.025	6.3	0.007	34.56	0	720,000	240,000
1/15/33	12 hr. specimen	480	1.017	6.3	0.004	17.28	120,000	1,080,000	360,000
1/16/33	12 hr. specimen	470	1.019	5.9	0.004	16.92	65,267	587,500	470,000

These 4 rheumatic subjects illustrate the relationship between changes in the urine and the onset of the rheumatic attack. The urinary changes in another patient are presented to illustrate their relation to the course of the disease throughout a period of months.

CASE 14.—C. M., a girl, aged 12, under observation since February, 1931, was admitted to the hospital with an attack of pancarditis accompanied by migrating pulmonary solidification. Following recovery she was given convalescent care at the Pelham Home, being discharged in excellent condition. On November 14, she contracted hemolytic streptococcic infection of the throat. On the fourteenth day after this, she was admitted to the Babies' Hospital with a rheumatic attack, the severity of which increased during the following six weeks. After three months of rest in bed, the process appeared to be subsiding. Tonsillectomy was performed on February 15. Sixty hours later the patient experienced a sharp recrudescence which was followed by recovery.

The urinary observations are presented in table 6.

This patient, with evidences of continued activity of the rheumatic process, had a constantly high urinary red blood cell count. With subsidence of the disease, the urine gradually became normal. After ton-

TABLE 6.—*Results of Examination of Urine in Case 14*

Date	Time of Taking Specimen, Hours	Volume, Cc.	Specific Gravity	p_H	Protein		Casts	Red Blood Cells	Epithelial Cells
					Per Cent	Amount, Mg.			
11/23/31	12	200	1.036	6.2	0.058	115.20	0	29,100,000	68,280,000
11/26/31	12	350	1.021	6.2	0.050	176.40	0	32,900,000	36,750,000
11/30/31	12	385	1.015	6.3	0.014	55.44	0	12,512,500	13,090,000
12/ 2/31	12	340	1.025	6.2	0.011	36.72	0	6,630,000	7,650,000
12/ 6/31	12	230	1.031	6.2	0.014	33.12	0	20,217,000	12,765,000
12/ 8/31	12	195	1.036	5.5	0.011	21.06	0	13,450,000	12,753,000
12/10/31	12	450	1.024	6.3	0.022	97.20	0	17,955,000	12,825,000
12/13/31	12	615	1.028	6.2	0.007	44.28	0	33,825,000	6,765,000
12/15/31	12	345	1.035	6.2	0.007	24.84	0	31,947,000	22,770,000
12/17/31	12	510	1.030	6.2	0.014	73.44	0	33,660,000	29,835,000
12/20/31	12	205	1.031	5.4	0.022	44.28	20,500	49,692,000	15,252,000
12/22/31	12	245	1.028	6.0	0.004	8.82	0	85,380,000	23,642,500
12/27/31	12	185	1.033	6.3	0.014	26.64	0	38,665,000	9,065,000
12/28/31	12	340	1.028	6.1	0.014	48.96	0	82,960,000	12,410,000
12/30/31	12	155	1.031	6.2	0.014	22.32	0	17,437,000	13,175,000
1/ 1/32	12	180	1.031	6.3	0.014	25.92	0	25,020,000	14,400,000
1/ 4/32	12	230	1.030	6.3	0.011	24.84	102,222	21,045,000	10,695,000
1/ 6/32	12	250	1.027	6.3	0.011	27.00	0	18,500,000	11,000,000
1/ 8/32	12	175	1.030	5.5	0.014	25.20	46,667	26,775,000	20,370,000
1/11/32	12	220	1.036	5.5	0.022	47.52	36,667	152,130,000	22,000,000
1/13/32	12	175	1.030	5.4	0.011	18.90	194,444	65,625,000	12,687,500
1/15/32	12	195	1.028	5.5	0.007	14.04	10,833	9,262,500	10,725,000
1/18/32	12	350	1.018	6.0	0.007	25.20	0	21,000,000	12,775,000
1/20/32	12	485	1.020	6.2	0.007	34.92	0	20,370,000	18,187,500
1/22/32	12	415	1.025	6.0	0.007	29.88	0	44,820,000	13,072,500
1/25/32	12	305	1.023	5.7	0.007	21.96	0	30,195,000	12,627,000
1/27/32	12	275	1.025	6.0	0.007	19.80	45,833	32,312,500	23,787,500
1/29/32	12	345	1.028	5.8	0.007	24.84	0	52,612,500	32,775,000
1/31/32	12	275	1.021	5.5	0.007	19.80	0	26,812,500	14,437,500
2/ 2/32	12	485	1.020	5.6	0.004	17.46	0	6,208,000	6,450,500
2/ 4/32	12	600	1.021	6.1	0.007	43.20	0	17,640,000	25,740,000
2/ 7/32	12	320	1.023	5.9	0.004	11.52	0	18,400,000	21,280,000
2/ 9/32	12	435	1.015	6.2	0.004	15.66	43,500	12,789,000	19,575,000
2/11/32	12	180	1.026	6.2	0.007	12.96	0	6,480,000	11,664,000
2/14/32	12	255	1.024	5.6	0.007	18.00	14,166	3,952,500	24,607,500
2/16/32	12	145	1.028	5.8	0.007	10.08	40,277	8,700,000	18,850,000
2/17/32	12	410	1.016	5.6	0.007	29.52	341,666	25,625,000	61,500,000
2/18/32	12	358	1.022	5.8	0.014	51.84	537,000	61,755,400	16,774,000
2/19/32	12	160	1.026	5.8	0.022	34.56	80,000	14,160,000	17,136,000
2/20/32	12	325	1.022	5.8	0.007	23.76	0	12,675,000	15,112,500
2/21/32	12	170	1.027	5.5	0.007	12.24	94,444	15,725,000	13,600,000
2/25/32	12	320	1.016	6.1	0.014	46.08	53,333	13,600,000	5,600,000
2/28/32	12	250	1.025	6.0	0.007	18.00	0	16,625,000	17,250,000
3/ 1/32	12	165	1.028	5.4	0.007	11.88	45,833	6,847,500	9,075,000
3/ 6/32	12	280	1.020	6.0	0.007	20.16	0	9,100,000	16,520,000
3/ 8/32	12	305	1.022	5.4	0.007	21.96	0	8,235,000	15,097,500
3/10/32	12	180	1.020	5.5	0.007	12.96	48,000	9,020,000	43,362,000
3/13/32	12	375	1.017	5.9	0.004	13.50	0	9,900,000	22,275,000
3/15/32	12	235	1.025	5.6	0.007	20.304	0	7,021,800	8,460,000
3/17/32	12	175	1.030	5.9	0.014	25.20	0	5,512,500	17,325,000
3/18/32	12	255	1.020	6.0	0.004	9.18	0	4,080,000	10,608,000
3/23/32	12	435	1.010	5.6	0.004	17.46	0	1,940,000	10,185,000
3/30/32	12	500	1.011	6.3	0.007	36.00	16,667	1,500,000	2,750,000
4/ 6/32	12	400	1.012	6.0	0.004	14.40	0	1,720,000	3,120,000
4/13/32	12	520	1.019	6.1	0.007	37.44	17,333	5,096,000	23,556,000
4/20/32	12	610	1.010	6.3	0.004	21.96	0	1,525,000	2,623,000
4/27/32	12	500	1.009	6.3	0.007	36.00	83,333	1,650,000	4,600,000
5/ 4/32	12	500	1.017	6.1	0.004	18.00	0	1,500,000	3,150,000
5/11/32	12	480	1.016	6.3	0.004	17.28	0	4,608,000	7,488,000
5/18/32	12	615	1.016	6.4	0.007	44.28	20,500	3,320,000	3,997,500
5/25/32	12	510	1.013	6.0	0.004	18.36	0	1,428,000	1,785,000
6/ 1/32	12	400	1.016	6.2	0.004	14.40	0	1,000,000	3,000,000
6/ 3/32	12	515	1.020	6.1	0.004	18.54	57,222	4,377,500	4,120,000
6/15/32	12	445	1.016	5.6	0.007	32.04	49,444	1,335,000	4,005,000
6/22/32	12	395	1.019	6.0	0.007	28.44	0	3,910,500	2,133,000
6/29/32	12	515	1.017	6.0	0.007	37.08	34,333	824,000	1,854,000

sillectomy (Feb. 15, 1932), there was a precipitous rise in the urinary red blood cell count, followed by an acute attack of rhematism. The disease then appeared to be quiescent for five months, and the urinary red blood cell count remained normal.

COMMENT

The 5 cases described in brief in part II illustrate the observations among children and young adults with acute rheumatism without congestive heart failure. Each patient was known to have rheumatism. Each contracted hemolytic streptococcic pharyngitis. Lyttle [16] found that nonrheumatic subjects following scarlatina or other hemolytic streptococcic diseases of the respiratory tract excreted, while symptom-free, a temporary shower of erythrocytes during the second or third week of convalescence. Between seven and twenty days after hemolytic streptococcic pharyngitis, a clinical change occurred in each rheumatic patient. In many cases this reaction was extremely mild, and in such instances (case 10) the shower of red blood cells was perhaps comparable to that observed in the nonrheumatic subject. In other cases (e. g., 11 and 14), following a similar infection, persistent hematuria minima developed, which paralleled somewhat the fluctuations in the activity of the disease. In a few instances (e. g., case 12), in addition to hemorrhage, the urinary observations suggested an inflammatory reaction in the kidneys. In these patients hematuria minima was not striking during the late stage of the disease, when specific nodules of the tendon sheath were detected, but began a few weeks after infection, at the time that a rise in the antibody titer was detected in the blood serum,[17] and appeared closely associated with the activity of the rheumatic process.

SUMMARY

When the rheumatic subject is infected with the hemolytic streptococcus, the initial response is of the usual clinical character.[18] If the infection is limited to the upper respiratory tract, recovery occurs within a few days. This illness, though mild, may nevertheless be the first phase in the development of a severe rheumatic attack.

Following the subsidence of the local infection, the patient usually regains his customary health, and nothing abnormal is detected clinically. This quiescent interval of days or a few weeks represents the second phase in the evolution of the rheumatic process. The second phase persists until a rise in the titer of immune bodies is detected in the blood of the peripheral circulation.[17] Almost simultaneously with this response

16. Lyttle, J.: J. Clin. Investigation **12**:95, 1933.

17. Coburn, A. F., and Pauli, R. H.: J. Exper. Med. **56**:651, 1932.

18. Coburn, A. F.: The Factor of Infection in the Rheumatic State, Baltimore, Williams & Wilkins Company, 1931.

of the immunity mechanism, the rheumatic process is activated in susceptible persons.

When the rheumatic process is activated, the initial response is characterized by manifestations of a hemorrhagic nature. Particularly common at this stage are epistaxis and the erythemas; while melena, hemoptysis and hematemesis also occur. Studies of the excretion of erythrocytes in the urine indicate the close relationship of hemorrhage to the activity of the rheumatic process. Late in the attack, when symptoms are subsiding and abnormal urinary observations have disappeared, there may be a second stage, characterized clinically perhaps only by the appearance of subcutaneous nodules.

When it was possible to study the tissues of patients dying during the initial cycle of a rheumatic attack, hemorrhagic lesions without distinctive histologic structure were conspicuous. The character of these nonspecific lesions suggested the activity of a single process with varying degrees of intensity: (1) engorgement of the blood vessels; (2) alteration in the permeability of the vascular tissues with diapedesis, but without a demonstrable change in the structure; (3) an inflammatory reaction. The damage to the tissue in the patients with acute rheumatism was characterized by the absence of detectable microorganisms and commonly by vasodilatation, swelling of the endothelium, necrosis of the collagen, infiltration with various wandering cells, and especially hemorrhage. During the first cycle of the rheumatic attack, few or no Aschoff bodies were detected in the cardiac muscle; however, the presence of specific lesions in the endocardium established the diagnosis.

Most of the rheumatic subjects in my group who died survived a prolonged illness of rheumatic fever. In these patients, hemorrhage was not conspicuous, and numerous Aschoff bodies were present in the cardiac muscle. The constant proximity of the Aschoff cells to necrotic collagen in these myocardial nodules suggests the process of healing.

In conclusion, the evolution of rheumatic fever consists of, first, a phase in which there is an infection of the respiratory tract with the hemolytic streptococcus; second, a symptom-free phase in which the immune response develops in the rheumatic subject,[3] and finally, the acute attack. During the third phase, activity of the rheumatic process is characterized clinically by a tendency to hemorrhage which is well correlated with the anatomic observations.

APPENDIX

ANATOMIC OBSERVATIONS IN CASES REPORTED

CASE 1.—*Gross Appearance.*—The peritoneal surfaces were free from exudate, but beneath the serosa of the mesenteries and parietal peritoneum, particularly that covering the posterior abdominal wall, were innumerable hemorrhages varying from 5 mm. to 6 cm. in diameter.

The heart was enlarged. On the inner surface of the pericardial sac were numerous subserous hemorrhages varying from less than 1 mm. to 17 mm. in width. The pericardial sac was bound to the epicardium by localized dense fibrous adhesions. Between the surfaces of the pericardium were deep red, somewhat gelatinous-looking masses of tissue from 2 to 3 cm. in length. The wall of the left auricle was thickened. Rows of tiny verrucae were present in the tricuspid, aortic and mitral valves. In addition, there was thickening of the aortic and mitral valves and of the chordae tendineae.

The coronary arteries, aorta, thymus and trachea were normal.

The posterior two thirds of the upper lobe of the right lung was purplish red and firmer than normal. One section appeared deep red, moist and satiny. The appearance of the posterior portions of both lobes of the left lung was similar to that of the deep red areas of the right lung. In the anterior portion were numerous hemorrhagic foci.

The tracheobronchial lymph glands were slightly enlarged.

The pulmonary artery was normal.

On the anterior and medial margins of the spleen was a row, 3.5 cm. long, of small, pearly gray cysts from 2 to 3 mm. in diameter.

The liver was enlarged.

The gallbladder, esophagus and stomach were normal.

The mucosa of the intestine showed many injected small vessels. The mesentery contained numerous small and large hemorrhages. The most extensive hemorrhage occurred along the vessels in the lower part of the colon.

The mesentery contained numerous subserous hemorrhages.

The suprarenal glands were normal.

In the peripelvic fat of both kidneys were scattered punctate hemorrhages.

The bladder and uterus were normal.

On section, hemorrhages were seen over the cut surface of both ovaries.

The brain was not examined.

Microscopic Examination.—The leaflet of the tricuspid value was thickened. Deep in its substance were foci in which there were swollen collagen fibers and a collection of cells, including lymphocytes, plasma cells, polymorphonuclears and Aschoff cells.

The aortic valve was thickened by a cellular hyaline connective tissue.

In the left ventricle the cardiac fibers were hypertrophied, and the nuclei were hyperchromatic. A large number of Aschoff bodies were present in the interstitial tissue, at the junction of the myocardium and the endocardium, and in the columnae carneae. In addition, there were regions in which extensive cellular infiltration had taken place between the fibers. In some the lymphocytes were most numerous, with plasma cells among them; in others polymorphonuclears appeared in large numbers. About some of the blood vessels there were scars extending into the muscle bundles. Collections of cells were seen in the subepicardial fat. In the columnae carneae there was complete destruction of the myocardial bundles with replacement by cellular accumulations and areas of hyaline connective tissue. The cardiac fibers at the margin of this area were atrophied, and there was an interstitial infiltration of cells.

The mitral valve was thickened by dense hyaline connective tissue; at the tip was a collection of fibroblasts and lymphocytes.

The endocardium of the left auricle was markedly thickened and divided into three zones. The widest zone was adjacent to the myocardium. In this zone were long swollen masses of collagen about which lay Aschoff cells. The greater part of this zone was composed of a cellular dense collagenous tissue in which

numerous blood vessels were growing perpendicular to the auricular surface. The middle zone was composed of collagen fibers between which were short rows of cells. The fibers ran parallel to the endocardial surface, and the cells were lymphocytes and Aschoff cells. The third zone was composed of collagen bundles cut transversely.

In the wall of the pericardial sac there was hemorrhage.

In the outer third of the media of the ascending aorta the collagen fibers were separated by rows of cells—lymphocytes, plasma cells, polymorphonuclear leukocytes and Aschoff cells. In the adventitia were several collections of Aschoff cells.

The intima of the pulmonary artery showed areas of thickening.

The malpighian bodies were sharply outlined. Hemorrhages were present in the spleen. The small cysts in the margin were lined by flattened cells.

About the efferent veins of the liver the sinusoids were injected, the hepatic cells were atrophied, and the cytoplasm was filled with fat vacuoles.

The pancreas was normal.

In the medulla of the suprarenal glands the capillaries were injected, and small foci of lymphocytes were seen.

In the pyramid of the kidneys were groups of injected capillaries. A small hemorrhage was present in the peripelvic fat.

The capillaries of the ovaries were congested, and small hemorrhages occurred in the stroma.

The uterus was normal.

In the serosa and the mesentery of the colon were numerous large and small hemorrhages.

Hemorrhage was present in the adipose tissue of the appendices epiploicae.

The lymph gland, thymus and striated muscle were normal.

There were areas in the upper lobes of the lungs in which many of the alveoli were filled with red blood cells, large mononuclear cells, coagulated fluid or masses of fibrin. Lining many of the alveoli was a heavy hyaline membrane. The alveolar walls were widened by intensely injected capillaries. In the lymphatics of the septums were masses of large mononuclear cells and erythrocytes. Some of the bronchi were lined by a hyalinized membrane.

CASE 2.—*Gross Appearance.*—The right pleural cavity contained 150 cc. of clear fluid. Fibrous adhesions were present between the upper lobe of the right lung and the parietal pleura.

The pericardial sac was bound to the sternum and to the ribs anteriorly by fibrous adhesions. The mediastinal tissues were edematous. The pericardial sac contained about 30 cc. of bloody fluid. The pericardial surfaces were covered with a fibrinous exudate which glued the heart to the pericardial sac, particularly in the basal region. The epicardial surface was covered with a thick, shaggy, fibrinous exudate which was undergoing organization over the left auricle, and in this portion numerous tiny capillaries could be seen penetrating into the exudate. The right auricle and ventricle were somewhat enlarged. On the infundibular leaflet and also the free border of the tricuspid valve were minute gray glistening vegetations at the line of closure. These did not extend as a continuous chain along the valve, but were found in small groups of from two to ten. Similar vegetations were present on the posterior leaflet. They did not extend on the chordae tendineae except in one instance, in which a delicate chorda from the posterior leaflet had from three to four minute elevations on it close to its attachment to the valve.

The aorta was normal.

The middle lobe of the right lung was stuck to the mediastinal pleura by a delicate fibrinous exudate which covered an area roughly 2.5 cm. in its greatest dimension. In the lower lobes of both lungs and in the middle lobe of the right lung were dark red areas, at times a lobule in extent. On closer inspection the red area was found to be made up of minute red dots, separated from each other by delicate gray bands, the whole giving an appearance similar to that of a hemangioma composed of tiny vessels with narrow gray septums between them. No definite areas of consolidation other than these were made out. This change was quite widespread in the three lobes mentioned.

Microscopic Examination.—The pericardium was covered by a thick fibrous exudate. The mesothelial cells of the epicardium had disappeared, and the collagen fibers next to the muscle were swollen. Many capillaries had grown into the inner layer of exudate, accompanied by lymphoid cells and fibroblasts, with a few polymorphonuclear leukocytes. At the outer boundary of this granulation tissue was a heavy infiltration of such leukocytes, many fibroblasts and here and there large basophilic cells with scant, indefinite cytoplasm, the giant pale nuclei and stellate nucleoli of which strongly suggested Aschoff cells. An unorganized exudate of fibrin, red cells and a few polymorphonuclears covered the outside of the section. No Aschoff bodies were seen in the myocardium, which appeared normal except for much extravasated blood between the muscle fibers.

A section was taken through folds of the endocardium just above the mitral valve. The auricular endocardium was greatly thickened, and its innermost layer was thrown up into ridges parallel with the valve ring. The ventricular endocardium, though not folded, was the seat of an intense reaction. The endothelium was intact, but immediately beneath it was an infiltration of cells with pyknotic, distorted nuclei, somewhat resembling connective tissue cells. They were often arranged in rows parallel to the surfaces, separating the swollen, deeply staining collagen fibers. The ridges were seen to be thickenings of this innermost layer and resembled small, recently organized vegetations, with many connective tissue nuclei perpendicular to the surface. Deeper down, the collagen fibers were swollen and disrupted and were thickly infiltrated with small pyknotic chromatic fragments and nuclei often distorted into sharp, angular shapes. Here and there were condensations of these fragments which resembled small focal necroses and which often seemed to push up the overlying endocardium in small elevations. Along the boundary between the muscle bundles and the endocardium was a zone of round cell infiltration, especially marked around the numerous small blood vessels. These areas sometimes looked like granulation tissue. Among the round cells could be seen a few polymorphonuclear leukocytes and some large basophilic cells which at times looked like fibroblasts and at times like Aschoff cells.

The myocardium appeared normal. The mitral leaflet showed the same roughening and thickening as the auricular endocardium.

In another section, the pericardium was as described. The pleura had fibrin over it, but the areolar tissue showed no changes.

The alveoli of the lungs were filled with an exudate composed mostly of red cells, with some fibrin and mononuclear cells. In other parts the exudate contained more fibrin and cells, but rarely many polymorphonuclears. The blood spaces contained little blood and often were collapsed. The alveolar septums were unusually cellular, and the intercellular material seemed swollen. The nuclei in the alveolar wall here and there took bizarre shapes, some having long tails, and others being shaped like a dumb-bell. The nuclei were often pyknotic and sometimes fragmented. In parts there was a suggestion of a hyaline membrane lining the alveoli. In a few places the fibrinous exudate was being invaded by strands of fibroblasts. The

bronchial mucosa was normal, and the submucosa was not infiltrated. There was some swelling of collagen beneath the pleura, and in places there were small collections of lymphoid cells around new capillaries, with an occasional polymorphonuclear cell. The mesothelial cells were swollen and in parts were gone.

Case 3.—*Gross Appearance.*—The serosa of the peritoneal cavity was smooth and glistening, but beneath it, particularly on the retroperitoneal wall, in the appendices epiploicae, over the sigmoid, in the mesentery and about the pelvic organs, were large numbers of small bright red hemorrhages. The largest hemorrhage did not exceed 5 mm. in diameter. The vessels about the hemorrhages were injected, particularly in the pelvis. There was no excess of free fluid, but in the posterior part of the pelvis were a few drops of blood-stained fluid, and the serosa on the posterior surface of the broad ligament contained many recent hemorrhages.

The thoracic cavity was normal.

There were numerous small bright red subepicardial hemorrhages, particularly over the right ventricle and the posterior surface of the left ventricle. There were three small petechial hemorrhages into the substance of the tricuspid valve near the base. The right ventricle was normal except for an occasional minute subendocardial petechia. The pulmonary cusps were thin and pliable. In the base of each was a small bright red hemorrhage. The mitral valve was striking. Along the free margin at the line of closure was an almost continuous row of heavy, though warty, yellow, opaque vegetations. The largest vegetation extended 3 cm, above the surface of the valve. A few of the vegetations contained small bright red hemorrhages. Both leaflets of the valve were slightly and diffusely thickened by connective tissue, and in the substance of the aortic leaflet several minute, engorged vessels were visible, extending from the base almost to the line of vegetations.

The aorta was normal.

The left lung weighed 144 Gm. The serosa was smooth and glistening. It contained a few small, bright red petechial hemorrhages, and beneath it, particularly over the posterior portion of the lower lobe, were many irregular, slightly depressed, reddish-purple areas, which on section were found to extend several millimeters into the parenchyma of the lung.

The spleen, liver, pancreas and suprarenal glands were normal.

In two of the pyramids of the kidneys was a yellow, opaque area, mottled with hemorrhage.

The cervix, tubes and ovaries were normal.

The small intestine was normal except for numerous small bright red hemorrhgaes beneath the serosa. Similar petechiae were present along the large intestine, as described. The terminal ileum and the ascending colon were congested.

The vessels over both cerebral hemispheres were congested, as were the dural sinuses. The pia-arachnoid was thin and translucent. A small cordlike mass, approximately 0.5 by 5 cm., of soft, elastic dark red blood clot lay free on the vertex of the brain, between the dura and the pia-arachnoid. The vessels over the vertex of both parietal lobes were particularly engorged, and there were small red discolorations in the pia-arachnoid about these vessels. On multiple coronal section, the brain presented a startling appearance. Scattered in the white matter of both cerebral hemispheres (rarely in the gray), in the corpus callosum, in both internal capsules, in the lenticular nuclei, in the cerebral peduncles, in the inferior and superior cerebellar peduncles, in the pons and, to a lesser extent, in the medulla and the upper cervical cord were many bright red hemorrhages. Most of the hemorrhages were from 0.5 to 2 mm. in diameter. The largest, however, in the white matter of the left occipital lobe, measured 2 by 3 cm. and extended anteroposteriorly for about 3 cm. The outer half of this hemorrhage was firm, dark red

and laminated; the inner part was soft and retracted from the occupied space after fixation. A somewhat smaller hemorrhage was seen in the right parietal lobe, and another in the left parietal lobe. The hemorrhages in the internal capsules tended to be confluent. The vessels, except for engorgement, appeared normal.

The middle ear and sinuses were normal.

Microscopic Examination.—About an occasional small myocardial vessel could be found a few large cells each with a deeply staining irregular ventricular nucleus and a large stellate hyperchromatic nucleolus. The cytoplasm of these cells was scanty and basophilic. About these vessels there was also a small amount of collagen, some fragments of which stained faintly basophilic. Rarely the collagen extended out between a few adjacent muscle fibers, partly replacing them. Just beneath the base of the mitral valve and toward the ventricular portion of the section some of the collagen fibers seemed to be more deeply eosinophilic than normal and rather swollen. About these fibers were many mononuclear cells, some of which had an irregular vesicular nucleus with a large nucleolus. There were also an occasional polymorphonuclear leukocyte and a few extravasated red cells. Similar mononuclear cells were seen in the valve substance. The surface of the valve bore a rheumatic vegetation composed of eosinophilic coagulum, into the base of which fibroblasts and mononuclear cells were growing. No bacteria could be seen on or in this vegetation. In the wall of a large coronary vessel there was a small collection of irregular mononuclear cells, a few of which had a large hyperchromatic nucleus with a stellate nucleolus. The nucleus of one of these cells was greatly elongated and distorted into an irregular fiber-like structure.

At one point of the aorta the intima was slightly thickened with a cellular accumulation composed chiefly of small irregular, angular and distorted hyperchromatic nuclei. Some of the nuclei were greatly elongated and were club-shaped. Others resembled polymorphonuclear leukocytes. An occasional large mononuclear cell was also present. In between these cells could be distinguished a rare swollen eosinophilic collagen fibril. The cells, however, tended to be arranged in longitudinal rows.

Most of the bronchi contained a dense polymorphonuclear exudate containing large numbers of bacteria. The walls of many of the bronchi were infiltrated with leukocytes, and in some the wall appeared to have been destroyed by the inflammatory process.

The pulp of the spleen was intensely hemorrhagic.

The liver, pancreas and suprarenal glands were normal.

As the tip of the renal papilla was approached, there was encountered an extensive diffuse hemorrhagic and polymorphonuclear inflammatory reaction, which separated the tubules in the pyramid and partly replaced them.

The superficial epithelium of the cervix was absent over a portion of the section at the site of an acute inflammatory process characterized by abundant hemorrhage and many polymorphonuclear leukocytes together with large masses of bacteria. This exudate covered the surface of the cervix at this point. The inflammatory zone was not deep, however, as it did not extend into the more superficial glands.

The ovaries were normal.

Most of the epithelium lining the esophagus had been replaced by an inflammatory exudate composed of dense bands of fibrin with scattered, fragmented and intact polymorphonuclear leukocytes. Large numbers of bacteria, chiefly cocci, were present in the exudate.

The small intestine and the large intestine were normal.

Between the ulcerations of the rectum, the mucous membrane was congested, and there were small hemorrhages.

The section of the appendices epiploicae contained a small hemorrhage into the fatty connective tissue.

The section of the left occipital lobe of the brain comprised a portion of an extensive hemorrhage, composed of red cells, clumps of fibrin and platelet columns, together with scattered groups of polymorphonuclear leukocytes, a few of which were fragmented. There was no cellular reaction about the periphery of this hemorrhage, as it infiltrated the surrounding substance of the brain. No vascular lesions could be made out. Adjacent to the hemorrhage, the substance of the brain was edematous in several places, and these edematous areas appeared continuous with distended Virchow-Robin spaces.

In the vertex of the right parietal lobe, the substance of the brain was essentially normal. The vessels of the overlying pia-arachnoid, however, were engorged, and there were several small extravasations of red cells.

Scattered throughout the section of the cerebral and superior cerebellar peduncles, particularly the latter, were many small, fresh petechial hemorrhages, spreading apart the adjacent nerve fibers. There was no cellular reaction about these hemorrhages. In some of them the red cells appeared to have fused together to form irregular hyaline masses. At one corner of the section was a portion of the wall of the aqueduct of Sylvius; it was normal.

Occasional small hemorrhages were scattered in the section of the medulla. The attached meninges were normal.

The right internal capsule and the adjacent lenticular nucleus contained extensive confluent areas of hemorrhage, with apparent interruption of many of the fiber tracts. The leukocytes present in the hemorrhages were for the most part intact.

There were several small hemorrhages scattered in the section of the cervical cord, particularly in the region of the nuclei. Except for congestion, the meninges were normal.

Case 4.—*Gross Appearance.*—A few small hemorrhages were present in the peritoneal fat. The rectus muscles were well developed and of good color. In the fascia between the rectus muscles many small dark red hemorrhages were present. The mesocolon and mesentery were thickly stippled with hemorrhages of various sizes. Many hemorrhages were present also in the omentum. They measured from 0.5 to 2 or 3 mm. in diameter, were apparently of the same age and were bright red.

The lower border of the liver was 5 cm. below the tip of the xiphoid process and 8 cm. below the costal margin in the right midclavicular line. The lower border of the spleen was approximately 2 cm. below the costal margin. The fat behind the peritoneum was likewise filled with hemorrhages, more numerous on the left side.

Some dense fibrous adhesions were present between the apex of the right lung and the parietal pleura. In the mediastinal fat were many hemorrhages similar to those described elsewhere. The pericardial sac contained approximately 100 cc. of pale greenish, slightly turbid fluid.

The epicardial and pericardial surfaces were covered with an irregular layer of fibrin. This fibrinous exudate varied in thickness from a few millimeters to from 4 to 5 mm. The exudate was more abundant over the posterior surface of the heart. Long strands of fibrin hung from the surface of the heart on the posterior surface backward to the pericardial sac. The exudate also was abundant over the base.

Above the posterior leaflet of the mitral valve and extending upward almost to the first part of the auricular appendage were yellowish streaks slightly elevated above the surrounding endocardial surface. Many small blood vessels could be made out in the mitral leaflets, particularly the aortic leaflet. They extended almost to the line of closure. They were especially numerous at the base of the valve. Above the line of closure of both leaflets was an almost continuous chain of tiny slightly opaque, yellowish vegetations. They projected above the surface of the valve approximately from 0.5 to 1 mm. The process was more marked on the posterior leaflet, which appeared distinctly edematous. The auricular surface of the posterior leaflet was altered; its whole surface seemed to be lifted. It was faintly yellow and had a gelatinous, semitransparent appearance. This change in the leaflet continued to the line of closure and stopped at the junction of the leaflet and the auricular endocardium. The chordae tendineae were somewhat thickened, those from the aortic leaflet to the anterior papillary muscle showing the most marked change. A small hemorrhage was present beneath the endocardium below the anterior leaflet of the aortic valve. This hemorrhage lay 0.5 cm. below the base of the cusp.

The aorta was normal.

The right lung was heavy, weighing 890 Gm. The upper and middle lobes were incompletely separated. Numerous hemorrhages were present in the pleura over the three lobes and particularly in the fissures between the lobes. Over the posterior and lower part of the lower lobe was a delicate fibrinous exudate. A similar exudate was present over the mediastinal surface of the upper lobe. Some of the same type of exudate was present on the diaphragmatic surface. The lung was boggy and at the same time had an elastic consistency. The lung was nowhere crepitant. The bronchi were filled with a great quantity of frothy fluid. On section, the cut surface was bathed in a considerable amount of this fluid. The surface of the right lung was somewhat variegated in appearance. In a few places it was light pink, and obviously the parenchyma in those portions contained air. The greater portion of the lung, however, was dark red and moist and did not present the obvious features of consolidation. The darker portion of the lung was slightly elevated above the air-containing part. In a few areas in the red portions, tiny yellow flecks were visible. On section of the lung, great edema was present in the anterior portion, apparently in the interlobar and alveolar septums, and small groups of lobules stood out in a surprising manner because of the widening of their septums. The bronchial mucosa was reddened. No exudate was made out on it. In the posterior part of the lung in the lower lobe, there was more air-containing parenchyma.

The spleen weighed about 240 Gm. and measured 13 by 3.5 cm.

The liver weighed 2,080 Gm. and measured 27 by 20 by 7 cm. The capsule was smooth. Through the capsule the parenchyma had a mottled yellow and reddish-purple appearance. On section, the lobules were found to stand out clearly; they were the same size throughout. The portion of the lobule around the efferent vein was sunken and dark red. The remainder of the lobule was brownish-yellow.

The gallbladder, pancreas, suprarenal glands, kidneys, bladder, prostate, seminal vesicles, testes, gastro-intestinal tract, duodenum, thymus, vessels and head were normal.

The pia over the vertex was edematous, the edema showing particularly well along the course of some of the vessels the walls of which had a gelatinous appearance. A few small hemorrhages were present in the pia, and in the pia over the vertex near the longitudinal sinus were tiny gray flecks which were too far

removed from the region of the sinus to be pacchionian granules. The tiny gray areas had sharp margins; the largest measured about 1.5 cm. in greatest diameter. They were quite clearly confined to the pia. They were present along the fissures of both frontal lobes, especially in the region of the superior frontal gyrus. The small hemorrhages and dilated capillaries were most numerous over the parietal gyri on either side.

Microscopic Examination.—The epicardial surface was covered with a layer of fibrin, varying in thickness, and containing only an occasional cell. The pericardium immediately beneath contained numerous blood vessels which were engorged and the endothelium of which was swollen and at times vacuolated. This layer was also edematous and infiltrated with a few polymorphonuclear leukocytes and wandering cells of all varieties. The infiltration extended into the adjacent myocardium for only a short distance. The cardiac muscle was somewhat variable in size. Some of the nuclei were large and irregular in outline, and contained an abundance of chromatin. Some of the muscle cells had vacuoles which stained faintly blue or not at all. The interstitial tissue was edematous. In some of the larger blood vessels the connective tissue seemed pushed apart to a considerable extent by the edema. No characteristic Aschoff bodies were found. At times the endothelium of some of the vessels was slightly swollen. In the wall of one of the larger arteries a few polymorphonuclear leukocytes and an occasional cell with a distorted nucleus were found.

Another section of the heart presented the features just described. In one of the connective tissue bundles a few polymorphonuclear leukocytes were found. In another area was an accumulation of cells with deeply staining nuclei suggestive, but not characteristic, of an early Aschoff body. Near another vessel were similar accumulations of cells.

In certain areas of the left auricle the endocardium was edematous. Small accumulations of distorted nuclei were found. In the endothelial layer were enncountered a few cells with deep blue nuclei arranged in a row parallel to the surface. At the junction of the myocardium and the endocardium were accumulations of small wandering cells. The interstitial tissue of the myocardium was edematous. The epicardial surface was covered with a layer of fibrin. A mass suggesting an Aschoff nodule was found in the epicardial fat.

The section of the mitral valve included part of the wall of the left ventricle. Near the line of closure of the valve was a vegetation composed of a somewhat hyalin-appearing granular material into which large fusiform cells were penetrating. A little closer to the tip of the valve was a collection of mononuclear cells with a few eosinophils just beneath the endothelium. In the depth of the valve close to the base were dense accumulations of mononuclear wandering cells of varying sizes, and an occasional polymorphonuclear cell. The capillaries were prominent, and their endothelium was swollen. Immediately over one of these accumulations the superficial part of the valve had a dense mass of mononuclear cells just under the endothelium. Still closer to the base of the valve was an area in which the connective tissue was fragmented, and about this were many nuclear particles. On the ventricular side of the valve, at its junction with the wall of the ventricles, was a superficial accumulation of all verieties of wandering cells, the small round cell predominating. There was some necrosis, for hyaline material was found in the central part of this mass. On the tip of one of the chordae tendineae was a subendothelial accumulation of mononuclear cells.

The muscle of the pericardium and the diaphragm did not show any definite changes except a small area of recent hemorrhage.

In a section through the mediastinal fat and the pericardium, the serosal cells had disappeared. On the surface was a thick layer of fibrin. The vessels in the deeper part of the pericardium were engorged, and their endothelium was swollen. A wide zone of edema with much fibrin was present at the junction of the pericardium and the mediastinal fat. Polymorphonuclear leukocytes and mononuclears were found in the zone. The edema extended out along the connective tissue septums between the lobules of fat. Some hemorrhages were present in the fat. A piece of parietal pleura contained in the section had a little fibrin on its surface, and beneath this fibrin the serosal cells had proliferated to form large masses. These cells were invading the fibrin.

On the surface of the parietal pleura was a great mass of proliferated serosal cells which seemed to have a stroma with them, as blood vessels were present. Many of the cells contained two or more nuclei, and some had as many as six. In certain portions of these cellular masses, polymorphonuclear leukocytes were found, and here and there were bands of fibrin. The fat beneath was undergoing serous atrophy, and in one portion was a dense infiltration by polymorphonuclears with bands of fibrin.

A few areas of nuclear depletion were found in the media of the aorta.

The pulmonary artery was normal.

Changes were widespread throughout the section of the lung. In some of the alveoli were fibrin, polymorphonuclear leukocytes and large mononuclear cells, and well preserved red cells were found. The alveoli so involved frequently formed irregular groups. The walls of the interalveolar septums were widened. They were edematous and infiltrated by wandering cells of all varieties. In other parts of this section the edema was more evident, with only scattered cells of the types just described in the alveolar spaces. Tightly adherent to the walls of the alveoli in the more edematous portions was a layer of hyaline material, usually of uneven thickness. A few of the alveoli contained almost nothing but a little fibrin and edema fluid. The epithelium covering their surfaces was distinctly prominent, and the cells seemed to be proliferating. The interlobular septums were tremendously widened owing to the edema fluid within them. The lymphatics were distended with fluid. Occasionally one of them was filled with polymorphonuclears.

Edema was more marked in another section of the lung than in the preceding one. The hyaline membranes against the alveolar sacs were distinct, but not so widespread. The acute inflammatory reaction within the alveoli was characterized by less marked engorgement. The interlobular septums were very edematous.

The fat surrounding the thymus was undergoing serous atrophy. The septums were edematous.

The sinuses of the spleen were engorged.

The changes in the liver were extreme. The cells around the efferent veins had undergone necrosis for a wide zone. They still remained as masses staining deeply with eosin and without nuclei. In these regions a few polymorphonuclear leukocytes had accumulated. The necrosis often extended through half the lobule and then ended abruptly, and well preserved hepatic cells were found in the remainder of the lobule. In some of the necrotic areas the blood had burst through the walls of the sinusoids. The connective tissue in the portal areas was not increased.

In the pancreas, aside from the edema of the interlobular septums, no alterations were made out.

The blood vessels in the zona reticularis were engorged.

The vessels of the kidney were engorged. The cells of the convoluted tubules were swollen, and the outline of the lumens of these tubules was often star-shaped.

The testes were normal.

The surface of the mucosa of the colon was covered with a thin layer of fibrinopurulent exudate. The vessels of the mucosa were engorged.

In a section of the lymph gland the vessels were engorged. The sinuses contained hemorrhage, with some polymorphonuclear cells and phagocytes which had engulfed red cells and small wandering cells.

The mesenteric fat had undergone serous atrophy.

CASE 5.—*Gross Appearance.*—Both ventricles were large, but the hypertrophy seemed more marked in the right one. The epicardium presented a few small petechial hemorrhages posteriorly near the auriculoventricular sulcus and also about the vessels at the base. On the posterior surface of the right auricle was a scanty finely granular pale exudate. The leaflets of the tricuspid valve were slightly edematous along the free margin. At the point where the anterior and medial leaflets join they were shortened and thickened by a small ridge of yellow translucent tissue which was slightly raised above the surrounding endocardium of the valve. The chordae tendineae were thin and delicate except near the area described, where they were somewhat shortened and thickened. The mitral ring was shortened. The valve was thickened along its free border and bore many small tough translucent slightly yellowish vegetations. These formed a continuous ring about the opening of the valve. Beneath them was a heavy ridge of fibrous tissue, but the valve was still freely movable. There were a few bright red hemorrhages into some of the vegetations. The chordae tendineae were markedly shortened. The papillar muscles were large. On the aortic cusps was again a practically continuous row of small tough pale yellow vegetations.

The aorta was normal.

The left lung was voluminous and crepitant, except over a few small depressed purple areas in the upper lobe and in the base of the lower lobe.

The right lung weighed 720 Gm. In general, it was similar to the left except that there were more numerous dark red somewhat firm areas in all three lobes.

The spleen was normal.

The liver and gallbladder weighed 1,630 Gm. The liver was flabby and dark purplish brown. The lobules were easily visible beneath the capsule; in most places they were unequal in size, being larger in the right lobe than in the left and appearing congested.

The pancreas was normal.

The left kidney weighed 200 Gm. It was firm and elastic. The capsule stripped easily, leaving a smooth dark red surface in which could be seen myriads of punctate hemorrhages. The stellate vessels were engorged. On section, the cortex presented an appearance similar to the external surface. The markings were irregular and partially obscured by many punctate hemorrhages. The background was grayish pink. Similar hemorrhages occurred throughout the medulla, and there were scattered petechiae in the mucosa of the pelvis. The outer surface of the kidney everted above the capsule. The vessels, both large and small, appeared normal except for congestion.

The right kidney weighed 215 Gm. It was otherwise entirely similar to the left.

The pelvic organs were normal.

Just above the ileocecal valve were a few bright red hemorrhages. There were similar hemorrhages into the mesentery.

Microscopic Examination.—Many of the muscle fibers of the heart were somewhat larger than normal and contained large well staining nuclei. About a rare coronary arteriole there was a very small amount of fibrous tissue replacing muscle

fibers. In one of these areas were several distended capillaries, and there were occasional large mononuclear cells. No Aschoff cells were seen, however. The endocardium at one point contained a small group of large mononuclear cells.

The myocardium of the left auricle was thickened, and there was an occasional hemorrhage in it. At one point the auricular endocardium was somewhat thickened. At this site there was an early rheumatic auriculitis. The collagen fibers were swollen, eosinophilic and fragmented, and between them were many scattered small cells with inconspicuous cytoplasm and chromatin-rich vesicular nuclei, each nucleus having a large irregular stellate nucleolus. Occasionally such cells had two nuclei with a small amount of neutrophilic cytoplasm. Here and there these cells were arranged in short rows between the collagen fibers. An occasional cell had an elongated bizarre nucleus, the long axis running at right angles to the surface of the auricle.

The tip of the mitral valve bore a rheumatic vegetation composed of amorphous deeply eosinophilic coagulum into the base of which numerous fibroblasts and large mononuclear cells were growing. The vegetation did not appear to be covered by endothelium. Beneath it the substance of the valve contained many fibroblasts, young blood vessels and plasma cells. There were also numerous scattered large mononuclear cells but no typical Aschoff cells. A small amount of refractile granular yellowish-brown pigment was present near the base of the vegetation. Opposite the vegetation the valve was composed of a loose network of fibroblasts, among which were numerous lymphocytes and large mononuclear cells. Toward the base of the valve there were many new large capillaries about which were scattered plasma cells and phagocytes. The substance of the valve appeared to contain an unusually large amount of hyalinized connective tissue.

The aorta was normal.

The section of the lung showed many red cells within the engorged blood vessels and in many of the alveoli. Mixed with the erythrocytes in many alveoli were numerous lymphocytes, some of which had angular, distorted nuclei, a few large mononuclear cells and many polymorphonuclear leukocytes.

The section was through one of the main bronchi near the hilus. Much of its mucous membrane had undergone squamous metaplasia. The wall was hyperemic and contained large numbers of leukocytes.

The sinusoids of the spleen were engorged, and in places the pulp was hemorrhagic.

The section of the liver presented the appearance of an advanced chronic passive congestion with marked engorgement of the sinusoids in the greater portion of each lobule. In many lobules the hepatic cells nearer the efferent vein had lost their nuclei and were necrotic. A few fat globules were seen. The portal areas were normal.

The pancreas and the suprarenal glands were normal.

The glomeruli of the kidneys were unusual in that they were practically bloodless, but the tufts were swollen and rich in cells. The nuclei were chiefly irregularly angular or oval and diffusely and deeply staining. They were chiefly within rather than on the surface of the tuft; that is, they were endothelial rather than epithelial. Occasionally one or two polymorphonuclear leukocytes could be distinguished in the tuft. Between some of the capillaries and also apparently within them could be seen strands of eosinophilic material. The capsular spaces were free from exudate, and there were no adhesions. In a few glomerular spaces were scattered erythrocytes, and the first portion of the convoluted tubule continuous with several glomeruli was filled with red cells. Throughout the section of the cortex and the medulla a majority of the tubules contained blood, sometimes

with a little granular coagulum and occasionally with a few polymorphonuclear cells. The tubular epithelium was normal. The vessels were normal except for marked congestion. Here and there the interstitial tissue was edematous and infiltrated with plasma cells, lymphocytes and large mononuclear cells. There was also a little interstitial hemorrhage, especially in the connective tissue of the pelvis.

In the mucosal stroma of the bladder were several areas of hemorrhage.

The prostate, testes and epididymis and thymus were normal.

CASE 6.—*Gross Appearance.*—There were numerous subpleural hemorrhages over all the lobes of the lungs.

The trachea, bronchi and lymph nodes were normal. The heart and spleen were enlarged. A few subcapsular hemorrhages were seen in the liver. The esophagus, stomach, intestine and suprarenal glands were normal. There were small hemorrhages in the renal cortex. The peritoneum, pancreas, mesenteric lymph nodes and thymus were normal. The brain was not examined.

Microscopic Appearance.—The endocardium of the auricle was thickened, and throughout it was a great increase in cells. The nuclei of these cells were distorted into bizarre shapes, and there was considerable fragmentation of the nuclei. They frequently lay perpendicular to wide eosinophilic bands, forming a palisade-like arrangement. No Aschoff bodies were present. The myocardial fibers immediately beneath the endocardium were vacuolated, and the interstitial tissue was infiltrated by polymorphonuclear leukocytes and lymphocytes, and there was some deposit of fibrin. In the interstitial tissue of the ventricle near the vessels there were collections of polymorphonuclear cells, lymphocytes and plasma cells. About some of the vessels were collections of cells resembling Aschoff cells, but they did not form typical Aschoff nodules.

In another section of the endocardium there was a small area in which the collagen fibers were fragmented and in which there was a localized collection of cells, lymphocytes and other cells of the Aschoff type. One of the columnae carneae was surrounded by an envelop of loosely packed connective tissue cells with collagen fibrils between them. In the myocardium about some of the vessels were groups of cells resembling the Aschoff type.

Many of the alveoli of the lungs contained coagulated fluid and large mononuclear cells.

The malpighian bodies in the spleen were large, and in the centers were accumulations of large eosinophilic cells with fragmentation of nuclei between them.

In a few of the portal spaces of the liver there were intensive changes in the walls of the small arteries. The lumen was much narrowed, and the media was in many instances practically replaced by a dense band of eosinophilic fibrinoid material in which lay a few fragmented nuclei. Around these arteries was a dense accumulation of small round cells and polymorphonuclear leukocytes. In one vessel the fibrinoid mass appeared to be between elevated endothelium and a muscle coat.

The thymus, pancreas, intestines, testes and epididymis were normal.

There were striking changes in the small arteries of the kidneys. Heavy eosinophilic masses of fibrinoid material replaced portions of the arterial walls, sometimes lifting the endothelium and sometimes replacing the muscularis, so that the entire muscle coat was replaced by this fibrinoid mass, which extended into the surrounding tissue. About such arteries there was a heavy accumulation of polymorphonuclear leukocytes and lymphocytes.

The glomeruli also showed extensive changes. Many showed hyaline thrombi in their capillaries and an infiltration of their tufts by polymorphonuclear leukocytes. In some there was a definite proliferation of capsular endothelium, producing crescent formation. Some capsular spaces were filled with red blood cells.

CASE 7.—*Gross Appearance.*—The small pieces of tissue removed at laparotomy for biopsy appeared to be composed chiefly of fatty tissue which was somewhat ecchymotic and covered with ecchymotic peritoneum on one surface. Within this tissue there were several yellowish-white, opaque areas that looked like areas of fat necrosis. The two larger pieces were twisted and irregular and appeared to be composed chiefly of fibrous tissue and a small amount of fat. They were markedly ecchymotic on the surface and partially covered with discolored fibrin. Multiple sections through this tissue showed it to be composed of fat and fibrous tissue and numerous ecchymoses. There appeared to be some rather yellowish-green fibrin in several areas.

The second specimen consisted of an appendix, which measured 2.5 cm. in length by 0.8 cm. in diameter. It was firm throughout. The subserosal vessels were slightly dilated in the distal half, and there was some clotted blood attached to the serosal surface of the proximal half. No fibrin was seen on the surface. On section, the lumen was patent in the proximal two thirds and rather wide; in the distal third it was patent but narrow. A small amount of greenish fluid material was found in the proximal portion of the lumen. One or two small ecchymoses were seen in the submucosa.

Microscopic Examination.—Nine different sections of the fatty tissue removed from above the bladder showed essentially the same picture throughout. Much of the fat was necrotic and appeared foamy or dead. Other portions of the fat were infiltrated by fibrin; a great number of round cells, plasma cells and polymorphonuclear leukocytes, some connective tissue and blood vessels were mixed with this tissue, and numerous fibroblasts could be seen extending throughout. The connective tissue showed considerable degeneration in most areas, and was highly infiltrated by inflammatory cells.

CASE 8.—*Gross Appearance.*—The specimen was an appendix measuring 6 by 0.75 cm., with a few fine adhesions on the serosal surface. On section, there was fibrosis of the wall; the lumen was filled with sanguineous material.

Microscopic Examination.—Sections of the appendix showed obliteration of the normal appendical architecture, the whole being replaced by fibrofatty tissue. Superimposed on this was an acute hemorrhagic picture with marked hemorrhagic exudate in the lumen.

The Department of Pathology of the Presbyterian Hospital and the Babies' Hospital generously placed their material at my disposal. Through their kindness, with the help of Dr. John Lyttle and Dr. Alwin M. Pappenheimer, and with the advice of Dr. Alphonse R. Dochez, it has been possible to conduct this study.

MENINGES IN INTRACRANIAL HEMORRHAGE OF THE NEW-BORN

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The literature on cerebral hemorrhage of the new-born concerns itself mainly with the size, source and mechanism of the hemorrhage, with but little attention to the reaction of the meninges and the brain. It was the latter phase of the condition that formed the basis for our investigations. In order to evaluate our work properly, we studied the brain and meninges grossly and microscopically. We also studied the question of the relation of atelectasis to intracranial hemorrhage. Special attention was paid to the occurrence of cerebral hemorrhage in three infants delivered by cesarean section.

LITERATURE

No attempt is made to review the literature on cerebral hemorrhage of the new-born in detail. The recent monograph of Ford [1] and the papers by Warwick [2] and Ylppö [3] give the more important references on the subject. Only papers dealing directly with the phase of the subject studied by us will be referred to.

Kaufmann [4] described the possibilities which might bring about intracranial hemorrhage in the new-born, but did not mention the histologic appearance of the meninges. Karsner,[5] in describing birth hemorrhage, did not mention the reaction of the meninges. Adami and

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1. Ford, F. R.: Birth Injuries of the Central Nervous System, Baltimore, Williams & Wilkins Company, 1927.

2. Warwick, M.: Necropsy Findings in New-Born Infants, Am. J. Dis. Child. **21**:488 (May) 1921; Cerebral Hemorrhage of the New-Born, Am. J. M. Sc. **158**:95, 1919.

3. Ylppö, I.: Pathologisch-anatomische Studien bei Frühgeborenen, Ztschr. f. Kinderh. **20**:212, 1919.

4. Kaufmann, E.: Spezielle pathologische Anatomie, eds. 7 and 8, Berlin, W. de Gruyter & Co., 1922.

5. Karsner, H. T.: Human Pathology, Philadelphia, J. B. Lippincott Company, 1926.

Nicholls [6] did not give any details as to possible changes of the meninges. Clein [7] described the microscopic changes which, according to him, give the typical microscopic picture of cerebral hemorrhage as follows:

> Underneath the arachnoid and in the pia a considerable amount of blood was found. Both layers of the pia were thickened as the result of the proliferation of large mononuclear cells, many of which contained phagocytic blood pigment. The capillaries of the pia were greatly dilated, but there was no hemorrhage immediately under the pia itself. The brain tissue was normal in appearance.

Chase,[8] recently, in a study of subdural hemorrhage associated with tentorial splitting in the new-born, described the histologic differences between the tentorium of a prematurely born infant and that of a full-term infant. However, he did not mention the histologic changes following the hemorrhage.

MATERIAL AND METHODS

Our series comprised forty-five new-born infants, twenty-five males and twenty females, in whom intracranial hemorrhage was found at necropsy. Two were stillborn, five were full-term and the rest were prematurely born. The age at death in the forty-three infants varied from 2 hours to 21 days.

In five cases the delivery was by forceps and in forty cases the birth was spontaneous. The three additional infants who were delivered by cesarean section will be discussed separately.

The cause of prematurity could not always be ascertained. In five cases the Wassermann test of the blood in either the father or the mother or both was positive. There were six twins, which fact may explain the prematurity in these. Arterial hypertension in the mother was the most likely cause in five more cases. In the twenty-nine remaining infants, no probable cause could be suggested.

During the same time in which the reported forty-five cases were observed, eighty-four other new-born infants came to autopsy who did not reveal intracranial hemorrhage, and these observations were used as controls.

Practically all the prematurely born infants in our series had attacks of intermittent cyanosis. Most of them were jaundiced, had a weak cry and were flaccid. Only one of them had twitchings.

The full-term babies had twitchings, moaned and had rigid extremities. Only one of the five had attacks of cyanosis.

In all the cases in which a lumbar puncture was done the fluid was either bloody or xanthochromic.

In all the examinations the brain was cut in situ, horizontally, in continuation with the circular section used for opening the skull as suggested by Kaufmann.[4] The upper portion of the cerebrum was then removed carefully from the dura, leaving the dura and the falx intact. The lower portion of the cerebrum was cut off from the cerebellum in the region of the brain stem and separated from the cerebellum so as not to injure the tentorium. This was done for the purpose of

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6. Adami, J. G., and Nicholls, A. G.: Principles of Pathology, Philadelphia, Lea & Febiger, 1909, vol. 2.

7. Clein, N. W.: Premature Infants, Am. J. Dis. Child. **37**:751 (April) 1929.

8. Chase, W. H.: An Anatomical Study of Subdural Hemorrhage Associated with Tentorial Splitting in the New-Born, Surg., Gynec. & Obst. **50**:31, 1930.

studying possible tears in the falx and tentorium and to rule out artefacts. Portions of the meninges and the brain from the region of the hemorrhage and also from other parts of the brain and meninges were hardened in a diluted solution of formaldehyde (1 : 10) and embedded in paraffin. The sections were stained with hematoxylin and eosin, with iron-hematoxylin and according to the van Gieson method for connective tissue. Mallory's glia stain was used in several instances. Frozen sections were cut occasionally, and were stained with sudan III.

RESULTS

The results are summarized in the accompanying tables.

Location of Hemorrhage.—In nineteen instances, the hemorrhage was confined to an area over the convexity of the brain; in ten the hemorrhage was found only in the region of the cerebellum and pons. Sixteen examinations showed a more or less diffuse hemorrhage. In fifteen instances a hemoventricle was found. A tear in the falx could be demonstrated four times. Tears in the tentorium were found in six other autopsies, and in one there was a tear in the wall of the longitudinal sinus.

Hemorrhage was always found in the subarachnoid space. In several instances the hemorrhage also was present in the subdural (epiarachnoid) space. It consisted of partly clotted, partly liquid blood which had adapted itself to the limited space and had formed, in most instances, thin layers of clotted blood. The blood clots in all the cases could be removed easily, leaving a smooth and glistening surface. In no instance was there evidence of early organization. The subarachnoid vessels were markedly hyperemic. In a large series of cases the subarachnoid space also showed extensive edema. The brain itself revealed a marked hyperemia in portions close to the hemorrhage. In only one of the forty-five autopsies was an extension of the hemorrhage into the brain tissue recognizable with the naked eye.

The three infants delivered by cesarean section were prematurely born and died at the ages of 3 hours, 4 hours and 9 days respectively. All three infants had a diffuse subdural (epiarachnoid) and subarachnoid hemorrhage extending over both hemispheres and also over the cerebellum. The hemorrhage over the latter area was especially marked in the second case, which also showed a slight extension of the hemorrhage into the adjacent cortical tissues. There was no sign of subcutaneous hemorrhage or evidence of caput succedaneum in any of the three cases.

Histologic Examination.—The histologic changes of the meninges in our cases were strikingly slight. None of the sections revealed a beginning organization of the hematoma. Even in the older infants no evidence was found of sprouting of vessels or beginning proliferation of connective tissues. The sections showed many red blood corpuscles,

TABLE 1.—*Observations at Autopsy in Forty-Five Cases*

Case	Age at Death	Meningeal Lesion	Location and Extent of Meningeal Hemorrhage	Microscopic Changes of Meninges	Brain	Lungs
1	Stillborn	Subarachnoid hemorrhage	Over right parietal lobe	Many red blood cells; a few endothelial cells	Hyperemia	Complete atelectasis
2	Stillborn	Subarachnoid hemorrhage	Diffuse	Many red blood cells; a few endothelial cells	Marked hyperemia	Complete atelectasis
3	3 days	Subarachnoid hemorrhage; edema	Diffuse	Many red blood cells; a few endothelial cells	Left lateral hemoventricle	Partial atelectasis
4	2 days	Tear in wall of longitudinal sinus; subdural and subarachnoid hemorrhage	Over left parietal lobe	Many red blood cells; occasional lymphocyte and endothelial cells	Normal	Small patches of atelectasis
5	5 days	Subarachnoid and subtentorial hemorrhage	Diffuse	Red blood cells	Right lateral hemoventricle; remnants of hemorrhage in brain	Normal
6	1 day	Tear of tentorium; subtentorial and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells	Right lateral hemoventricle; marked hyperemia of cerebellum	Partial atelectasis
7	10 days	Tear in falx; subdural and subarachnoid hemorrhage	Over left cerebral hemisphere	Red blood cells and occasional endothelial cells, with phagocytosed red blood cells	Normal	Patchy atelectasis and bronchopneumonia
8	5 days	Tear of tentorium; subdural and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells	Right lateral hemoventricle; marked hyperemia of cerebellum	Partial atelectasis
9	14 days	Subdural hemorrhage and subarachnoid hemorrhage (slight)	Diffuse	Many red blood cells; endothelial cells with phagocytosed red blood cells	Left lateral hemoventricle	Bronchopneumonia
10	2 days	Subarachnoid and subtentorial hemorrhage	Around pons and cord	Many red blood cells; occasional endothelial and lymphocytes	No change	Partial atelectasis
11	1 day	Subdural and subarachnoid hemorrhage	Over cerebral hemispheres	Marked hyperemia; red blood cells; a few endothelial cells	No change	Partial atelectasis
12	3 days	Subarachnoid hemorrhage; marked hyperemia	Diffuse but mainly over cerebellum	Many red blood cells; endothelial cells	Hyperemia	Partial atelectasis
13	1 day	Subarachnoid hemorrhage	Diffuse	Red blood cells; a few endothelial cells	Hyperemia of cerebrum	Little atelectasis

14	25 hours	Tear of tentorium; subarachnoid and subdural hemorrhage; marked hyperemia	Diffuse	Red blood cells; a few endothelial cells; no reaction	Bilateral hemoventricle	Partial atelectasis
15	3 hours	Tear in falx; subdural and subarachnoid hemorrhage	Diffuse	Red blood cells; a few endothelial cells	Bilateral hemoventricle; hyperemia	Marked atelectasis
16	6 hours	Subdural and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells; no reaction	Marked hyperemia	Atelectasis and early bronchopneumonia
17	6 days	Subdural and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells; no reaction	Left lateral hemoventricle	Some atelectasis; bronchopneumonia
18	8 hours	Subarachnoid hemorrhage	Diffuse	Red blood cells; no reaction	Bilateral hemoventricle	Partial atelectasis
19	14 days	Subdural hemorrhage	Over cerebral hemispheres	Many red blood cells; endothelial cells with phagocytosed red blood cells	No change	Organizing bronchopneumonia
20	2 days	Subdural and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells and few lymphocytes	Slight left hemoventricle	Partial atelectasis; early bronchopneumonia
21	2 days	Subdural and subarachnoid hemorrhage	Over right occipital lobe	Many red blood cells; few lymphocytes	Red blood cells in brain tissue	Slight atelectasis
22	14 hours	Tear of falx; subdural and subarachnoid hemorrhage	Diffuse	Hyperemia; many red blood cells; pigmented endothelial cells	Left lateral hemoventricle (slight)	Partial atelectasis
23	12 hours	Tear in falx; subdural and subarachnoid hemorrhage	Over cerebral hemispheres	Many red blood cells; a few endothelial cells	Bilateral hemoventricle (slight)	Partial atelectasis
24	15 hours	Marked hyperemia; slight hemorrhage	Over right lobe of cerebellum and pons	Red blood cells	No change	Partial atelectasis; bronchopneumonia
25	6 hours	Subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells	No change	Partial atelectasis
26	2 days	Subarachnoid and subdural hemorrhage	Over both cerebral hemispheres	Very many red blood cells; a few endothelial cells	No change	Partial atelectasis
27	2 days	Subdural and subarachnoid hemorrhage	Diffuse	Many red blood cells	Marked hyperemia	Atelectasis except in right middle lobe
28	2 days	Subdural hemorrhage	Over both cerebral hemispheres	Many red blood cells	Right lateral hemoventricle	Partial atelectasis
29	2 hours	Marked hyperemia and subarachnoid hemorrhage	Over both cerebral hemispheres	Marked hyperemia; red blood cells	Normal	Marked atelectasis
30	21 days	Older remnant of hemorrhage in subarachnoid space	Over left parietal lobe	Red blood cells; a few lymphocytes and endothelial cells with phagocytosed red blood cells	Normal	Normal
31	2 days	Subarachnoid and subdural hemorrhage	Diffuse	Many red blood cells	Hyperemia	Partial atelectasis
32	4 hours	Tear of tentorium; subarachnoid and subdural hemorrhage; also epidural hemorrhage	Diffuse	Red blood cells; lymphocytes; endothelial cells; no polymorphonuclear leukocytes	Right lateral hemoventricle; hyperemia	Little atelectasis

TABLE 1.—*Observations at Autopsy in Forty-Five Cases—Continued*

Case	Age at Death	Meningeal Lesion	Location and Extent of Meningeal Hemorrhage	Microscopic Changes of Meninges	Brain	Lungs
33	5 hours	Tear of tentorium; subarachnoid and subdural hemorrhage	Diffuse	Red blood cells	Hyperemia	Partial atelectasis
34	2 days	Subdural hemorrhage	Over occipital lobes	Red blood cells; occasional lymphocytes; endothelial cells	Normal	Partial atelectasis
35	21 hours	Subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells	Hyperemia	Marked atelectasis
36	22 hours	Subdural and subarachnoid hemorrhage	Diffuse	Red blood cells; a few endothelial cells and occasional lymphocytes	Normal	Normal
37	2 days	Subarachnoid hemorrhage	Diffuse	Red blood cells; a few endothelial cells and occasional lymphocytes	Hyperemia	Partial atelectasis
38	1 day	Tear of tentorium; subdural and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells; a few lymphocytes and endothelial cells	Hyperemia	Almost complete atelectasis
39	3 days	Subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells; occasional lymphocytes and endothelial cells	Bilateral hemoventricle; hyperemia	Partial atelectasis
40	16 hours	Subdural and subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells; occasional lymphocytes and endothelial cells	Hyperemia	Partial atelectasis
41	12 hours	Subdural and subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells; occasional lymphocytes and endothelial cells	Hyperemia	Partial atelectasis
42	2 days	Subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells; occasional polymorponuclear leukocytes and lymphocytes	Hyperemia	Almost complete atelectasis
43	4 hours	Subarachnoid hemorrhage	Over cerebral hemispheres	Red blood cells	Normal	Partial atelectasis of both lungs
44	9 days	Subdural and subarachnoid hemorrhage	Around cerebellum and pons	Red blood cells	Hyperemia of cerebellum	Few atelectatic portions
45	5 hours	Subdural and subarachnoid hemorrhage	Over cerebellum, pons and cord	Many red blood cells; massive hemorrhage	Hyperemia; red blood cells in brain tissue	Almost complete atelectasis

reddish-brown pigment granules and serum in the subarachnoid space. Occasionally, a few polymorphonuclear leukocytes, lymphocytes and endothelial cells could be made out. Some of the latter contained pigment granules. All the blood vessels in the subarachnoid space were markedly hyperemic. Some of the fields showed a varying amount of an edema-like material. The lining cells of the arachnoid and dura mater presented no changes.

The sections taken from the gray and white matter of the brain in the region of the subarachnoid hemorrhage showed many distended vessels, which were filled with red blood corpuscles. These were more pronounced in the cerebellum. Three brains also revealed the extravasation of red blood corpuscles in areas surrounding hyperemic blood vessels. In only one of these three cases was there a more severe hemorrhage into the brain itself. The sections in this case revealed the presence of red blood corpuscles within the brain and a slight destruction of brain tissue, but did not disclose a noticeable reaction in the surrounding tissue.

TABLE 2.—*Location of Intracranial Hemorrhage in Forty-Five Cases*

Location of Hemorrhage	Number of Cases
Convexity of the brain	19
Around cerebellum and pons	10
Diffuse	16

Thirty-nine cases showed a partial atelectasis of the lung. In seven of these cases the atelectasis was extensive. In only two cases was it complete. Seven cases revealed a bronchopneumonia.

COMMENT

The outstanding result of the study of our material is the almost complete lack of evidence of any reaction of the meninges due to hemorrhage. Some of the sections showed a few endothelial cells carrying blood pigment. In some instances there were found occasional lymphocytes and polymorphonuclear leukocytes, but none of the sections revealed any evidence of early organization, even though some of the infants remained alive for several weeks. The histologic picture was the same in full-term and in prematurely born infants. We believe that the lack of meningeal reaction might be explained by the possibility that the hemorrhage was in the stage of absorption rather than in the stage of organization.

It might be mentioned in this connection that Hatschek,[9] in a recent communication, reported the absence of organization in some cephalo-

9. Hatschek, O.: Zur Histologie des Kephalhämatoms, Beitr. z. path. Anat. u. z. allg. Path. **82**:268, 1929.

hematomas. He maintained that it depends on the presence of serum surrounding the hematoma whether or not organization occurs. In case the hematoma is surrounded by serum, organization does not occur, but the hematoma in time will be surrounded by a connective tissue capsule. If, however, serum is not present, the hematoma will be organized and finally be replaced by connective tissue. The same conditions prevail in external and internal (epidural) cephalohematoma. In all our material, serum and edema were noted surrounding the areas of hemorrhage. This may account for the lack of organization. On the other hand,

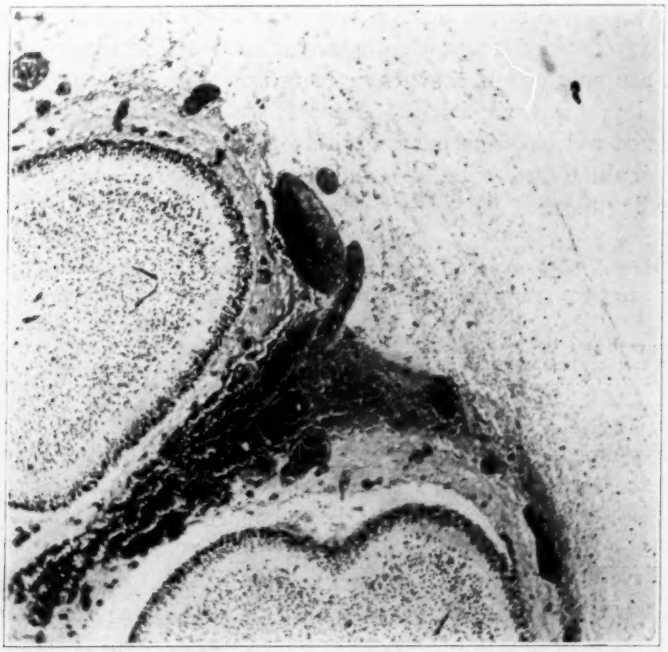

Fig. 1.—Subarachnoid hemorrhage in the region of the cerebellum in a patient who died six days after birth. Note the presence of red cells and the absence of other cellular elements. Iron-hematoxylin-eosin; × 80.

none of the cases showed an attempt at encapsulation of the hemorrhage. The dura and arachnoidea apparently do not respond with the formation of a capsule as readily as do other structures.

The lack of meningeal reaction in our series may explain why comparatively few children later in life manifest any effects from cerebral hemorrhage occurring at birth. A combined study of necropsies, clinical histories and changes in the cerebrospinal fluid indicates that this condition occurs not infrequently in the new-born, but not always with gross symptoms. It is difficult to reconcile the apparent frequency of the

occurrence of this lesion with the infrequency of symptoms in both early and later life. The following comment will illustrate our point.

During the same time in which the forty-five cases reported here were studied, eighty-four other new-born infants who came to autopsy did not reveal any evidence of intracranial hemorrhage. Therefore, of the one hundred and twenty-nine infants, forty-five or 37.5 per cent showed intracranial hemorrhage. Hess, Chamberlain and Lundeen[10] found intracranial hemorrhage in eighty of the two hundred and three prematurely born infants who came to autopsy, or in 39.4 per cent. It should

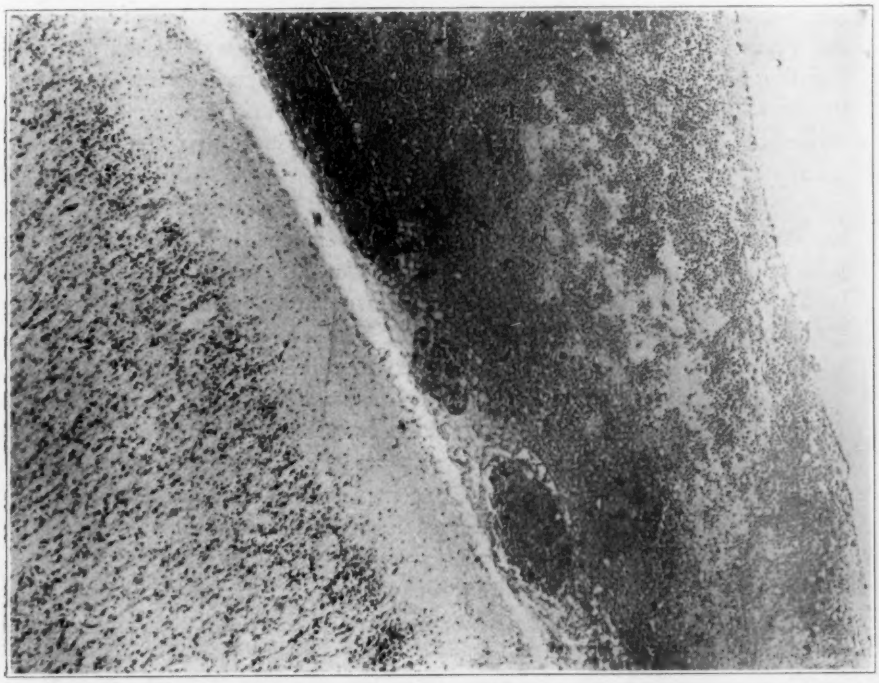

Fig. 2.—Section of the subarachnoid space and brain in a patient who died five days after birth. Note the large amount of red cells and the absence of any noteworthy reaction. Iron-hematoxylin-eosin; × 160.

be taken into consideration that the patients of the authors mentioned, as well as most of our patients, were premature infants.

Necropsy statistics alone, however, cannot be taken as criteria as to the frequency of intracranial hemorrhage, because the number of infants with intracranial hemorrhage who remain alive is not taken into consideration, nor are clinical symptoms alone always diagnostic of intra-

10. Hess, J. H.; Chamberlain, I. M., and Lundeen, E. C.: Premature Infants: Report of 761 Consecutive Cases, Pennsylvania M. J. **33**:429, 1930.

cranial hemorrhage. It is well known that children suffering from meningeal hemorrhages may not show any immediate clinical symptoms, and late manifestations may be due to changes in the brain other than cerebral hemorrhage. Up to the present date, the changes in the cerebrospinal fluid in cerebral hemorrhage are also not characteristic enough to allow the making of an absolute diagnosis of intracranial hemorrhage, although such a diagnosis might be inferred from an examination of the fluid. According to Sharpe and Maclaire,[11] who consider a bloody cerebrospinal fluid an indication of cerebral hemorrhage, the incidence of cerebral hemorrhage is 9 per cent of all new-born infants. However, if xanthochromia or a yellow discoloration of cerebrospinal fluid is taken as evidence of meningeal hemorrhage of the new-born as is stated by Fleming and Morton [12] and by Kutscher,[13] the incidence of intracranial hemorrhage in some form is very high, as xanthochromia was found frequently in the series of cases studied by Levinson, Greengard and Lifvendahl [14] and by Glaser.[15]

Enough evidence has been presented in the literature quoted to indicate that intracranial hemorrhage in the new-born (both full-term and premature) is not an uncommon occurrence and may be present in 9 per cent of all new-born infants (Sharpe and Maclaire [11]). Even though this condition cannot always be diagnosed with certainty during life, many times there is no doubt as to the diagnosis. Some of these infants not only survive but develop into normal children. Fleming and Morton, for instance, stated that many infants with severe injury to the head at birth made perfect recoveries and showed no sequelae. They further mentioned that in thirty-three instances of intracranial hemorrhage, when the children were seen again after a year or later, only five had mental or physical defects, and it was not at all clear whether these defects were the result of intracranial hemorrhage or of other causes.

The question naturally arises as to why more children do not have symptoms which can be traced back to a cerebral hemorrhage occurring at birth. Since we have not found any noteworthy reaction of the meninges in our series, it seems likely that in many instances of intracranial hemorrhage the hematoma is completely absorbed without leaving any residue. If, however, organization of the hematoma with subsequent

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11. Sharpe, W., and Maclaire, A. S.: Intracranial Hemorrhage in the New-Born, J. A. M. A. **86**:332 (Jan. 30) 1926; Am. J. Obst. & Gynec. **9**:432, 1925.

12. Fleming, G. B., and Morton, E. D.: Meningeal Hemorrhage in the New-Born, Arch. Dis. Childhood **5**:361, 1930.

13. Kutscher, G. W., Jr.: Cistern Puncture in Infants, Am. J. Dis. Child. **42**: 1428 (Dec.) 1931.

14. Levinson, A.; Greengard, J., and Lifvendahl, R. I.: Cerebrospinal Fluid in the New-Born, Am. J. Dis. Child. **32**:208 (Aug.) 1926.

15. Glaser, J.: Cerebrospinal Fluid of Premature Infants, Am. J. Dis. Child. **36**:195 (Aug.) 1928.

fibrous replacement occurred, it would make it difficult to understand why only a few children show lesions afterward which can be interpreted with certainty as the direct result of an intracranial hemorrhage occurring, apparently, during delivery.

The three cases of intracranial hemorrhage which were found at autopsy in new-born infants delivered by cesarean section are especially noteworthy from the standpoint of their etiology because trauma could be ruled out in these cases as the causative agent. There was no evidence of syphilis in the mothers of these three infants. No forceps were used. The hemorrhage was not multiple in the meninges or brain nor was there a complete atelectasis in any of these cases, which possibly could have explained the hemorrhage on the basis of asphyxia. No petechiae were found in other serous membranes which might have been caused by a blood dyscrasia, although one of the cases showed petechial hemorrhages in the thymus and the lungs. All three infants, however, were prematurely born. Two of them also were deeply jaundiced. The cesarean section was performed because of toxemia of the mother during pregnancy.

We believe that toxemia of pregnancy was either the chief or the contributory factor in the causation of the intracranial hemorrhage in these three infants delivered by cesarean section. Whether these cases belong in the group showing hemorrhage in utero before labor, as described by Cotard, Gibb and Osler,[16] or whether the hemorrhage was produced during labor as a result of the difference between intra-uterine and extra-uterine atmospheric pressure, we cannot say. It might be mentioned in this connection that among the eighty-four infants who came to autopsy during the same time as those in the series studied, there were three infants who also were delivered by cesarean section. None of these revealed any intracranial hemorrhage.

As mentioned previously, one of the reasons for studying the cases reported here was to see whether or not any relationship could be demonstrated between intracranial hemorrhage and atelectasis. Most of our necropsies revealed partial atelectasis. The lungs of a few infants in which atelectasis could not be detected were the seat of a bronchopneumonia. It is, of course, possible that in these cases atelectasis preceded the bronchopneumonia. Most of the eighty-four new-born infants who came under our observation during the time in which the cases reported were encountered and who did not have any intracranial hemorrhage also had some degree of atelectasis. Three of our cases of intracranial hemorrhage showed neither atelectasis nor evidence of pneumonia. In this series, therefore, we could not find any relation between atelectasis and intracranial hemorrhage.

16. Cotard, Gibb and Osler, quoted by Ford.[1]

SUMMARY

1. In forty-five cases of intracranial hemorrhage in the new-born there was a striking lack of cellular reaction in the meninges.

2. We believe that the small number of clinically evidenced complications of intracranial hemorrhage in children who survive can be explained by the absorption of the hematoma without organization and without the formation of a fibrous scar.

3. Three instances of intracranial hemorrhage in our series occurred in premature infants delivered by cesarean section, indicating that trauma was not the principal cause of intracranial hemorrhage. In these infants, maternal toxemia seemed a possible contributory cause of the hemorrhage.

4. There was no relationship between intracranial hemorrhage and atelectasis in our series.

EFFECT ON PEPTIC DIGESTION IN VITRO OF ARTIFICIAL FEEDING AS USED FOR AMERICAN INFANTS

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Two important scientific articles concerned with the feeding of infants have appeared in *The Journal of the American Medical Association,* "Peptic Digestion of Cow's Milk," by Hess, Koch and Sennewald,[1] and "Protein Digestion in Infancy," by Ernst Freudenberg.[2] In order to add a little, if possible, to the information reported in these articles, this comparative study of the effect of various modifications of cow's milk on peptic digestion in vitro has been made. Milk mixtures not previously reported on have been included. Diluted feedings rather than whole milk have been used, with conditions set near the optimum for peptic activity. Increase of milligrams of amino-nitrogen resulting from peptic digestion has been ascertained and the increase per gram of protein calculated as the basis of comparison for digestion by pepsin.

The feedings listed have been made up and digested with pepsin. Unless otherwise stated, ordinary pasteurized mixed Holstein Ayrshire market milk was used, and the milk was diluted with water in the ratio of 2:1. Evaporated milk and dried milk were diluted first to approximate the protein content of whole milk and then further diluted with water, 2:1. All additions were incorporated as or in the one-third diluent.

The figures reported in this article have been taken from the thesis submitted to the Graduate School of Cornell University in partial fulfilment of the requirements for the degree of doctor of philosophy.

The feedings of cow's milk which have been studied are as follows:

Simple dilutions:
- One part milk to one part water
- Two parts milk to one part water
- Whole milk

Raw milk:

Heat treated milk:
- Pasteurized
- Boiled
- Evaporated
- Dried

1. Hess, J. H.; Koch, E. M., and Sennewald, Z. C.: Peptic Digestion of Cow's Milk, J. A. M. A. **87**:1360 (Oct. 23) 1926.

2. Freudenberg, Ernst: Protein Digestion in Infancy, J. A. M. A. **93**:1208 (Oct. 19) 1929.

Carbohydrate additions:
- Cereals
  - Oatmeal water
  - Wheatena water
  - Barley flour gruel
- Sugars
  - Sucrose
  - Dextrimaltose, numbers 1, 2, 3
- Banana

Milk high in fat, Guernsey

Acid additions:
- Hydrochloric
- Lactic
- Acetic
- Citric
- Lemon juice
- Orange juice
- Tomato juice, canned

Alkaline additions:
- Sodium bicarbonate
- Sodium citrate
- Lime water

Miscellaneous additions:
- Gelatin
- Egg yolk, with and without lemon juice
- Browned butter and flour mixture

Altered protein:
- Whey
- Protein milk

METHOD

After many trials the following procedures for estimating peptic digestion were found satisfactory. Five cc. of 1 per cent pepsin solution made of Parke Davis 1:3,000 powdered pepsin and 15 cc. of tenth normal hydrochloric acid were added to 15 cc. of the feedings, with additions in the order of (1) feeding, (2) pepsin and (3) hydrochloric acid. Small Erlenmeyer flasks were used. The flasks were strongly rotated by hand after each addition. Every effort was made to work rapidly and to control the temperature, especially when the undigested blank samples were handled, for which solutions were iced. The digestion mixtures were incubated for four hours at 38 C. All the samples were prepared for titration by the method of Leary and Sheib,[3] which was slightly modified. Titration with sodium hydroxide in the presence of formaldehyde was used to determine the actual breakdown of peptide linkages, and the amino-nitrogen produced by digestion of the feedings was calculated. The Kjeldahl method[4] was used to determine the nitrogen content, which was multiplied by 6.38[5] to get

3. Leary, J. T., and Sheib, S. H.: Gastric Digestion of Milk Proteins, J. Biol. Chem. **28**:393, 1917.

4. Sumner, J. B.: Laboratory Experiments in Biochemistry, Ithaca, N. Y., Cornell Medical College, 1928 and 1929, p. 58.

5. Leach, Albert: Food Inspection and Analysis, ed. 3, New York, John Wiley & Sons, 1914, p. 145.

the milk protein. Finally the milligrams of amino-nitrogen resulting from the four hours of digestion were calculated per gram of protein as a more exact basis of comparison than the milligrams of nitrogen per gram or cubic centimeter of milk mixture. The quinhydrone electrode was used in determining the p_H of the digestion mixtures.

By adding the pepsin before the acid, the clotting or rennet action of the pepsin was utilized, and the pepsin was exposed to the favorable or unfavorable effect of the feeding, without previous protection of the pepsin by acidification with hydrochloric acid. The p_H of the digestion mixture resulting from the amounts of materials used was close to p_H 2 for a simple feeding of cow's milk diluted with water in a ratio of 2:1. Freudenberg [6] has pointed out that a low p_H and peptic digestion are possible in the infant, and as the aim of the study was to compare the effect of the feedings on the protein digestion by pepsin, a more acid p_H range nearer the optimum for enzymatic action than that previously used [7] was decided on. Further, the efficiency of the mixtures in promoting peptic activity, both directly and indirectly, through acid-sparing properties was considered a sounder means toward evaluating their worth in this respect than bringing them all to the same p_H with different amounts of acid.

RESULTS

The entire method as outlined here was found satisfactory for obtaining good grossly comparative results which could be repeated day after day when similar mixtures were digested. Only marked differences, however, should be considered in evaluating results of peptic digestion, first, because there is some variation in the digestion itself, and, secondly, because the differences obtained are exceedingly small in peptic digestion.

In considering simple dilutions of milk, it was found that the digestibility, that is, the milligrams of nitrogen produced per gram of protein, varied to a very small extent, even though the dilution much increased the hydrogen ion concentration. Apparently the favorable effect of a higher concentration of protein on the peptic digestion of whole milk greatly offset the unfavorable effect of the more alkaline p_H, as compared with diluted milk, as shown in table 1.

The differences in the effect of heating and evaporating milk were also small, as shown in table 2. Dried milk seemed somewhat more digestible, but because such differences may be within experimental error, I again urge the necessity of taking only marked differences into account in estimating the results of experiments on digestion, even when they are determined as exactly as possible, in vitro. There was no effect, to speak of, on the p_H of the digestion mixture.

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6. Freudenberg, Ernst: Physiologie und Pathologie der Verdauung im Säuglingsalter, Berlin, Julius Springer, 1929, pp. 59, 94.

7. Hess, J. H.; Koch, E. M., and Sennewald, Z. C.: Peptic Digestion of Cow's Milk, J. A. M. A. **87**:1360 (Oct. 23) 1926.

Addition of carbohydrates brought out the effect on peptic digestion of thickness of mixture, with adsorption of the enzyme by the particles of carbohydrates in suspension, which reduced the activity of the pepsin even when there was no unfavorable effect on the p_H, as is shown by the typical figures in table 3.

As will be observed, additions of barley flour and banana, which produced definitely thicker mixtures, were definitely less digestible by pepsin than mixtures with additions of clear cereal water and of soluble sugars. Lactose, which was hard to dissolve, depressed peptic activity somewhat.

TABLE 1.—*The Effect of Simply Diluting Milk on Digestion by Pepsin*

Feeding	Sample	Gm. of Protein per Fluid Ounce of 30 Cc.	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Cow's milk mixed, pasteurized, undiluted.....	A	0.950	16.50	2.9
	B	0.950	16.87	2.9
Simple dilution of cow's milk				
Dilution: 2 parts milk, 1 part water.....	A	0.652	18.53	2.1
	B	0.649	18.53	2.1
Dilution: 1 part milk, 1 part water.....	A	0.475	18.23	1.8
	B	0.475	17.49	1.8

TABLE 2.—*The Effect of Heating and Drying Milk on Digestion by Pepsin* *

Feeding	Sample	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Mixed pasteurized cow's milk.....	A	18.53	2.1
	B	18.53	2.1
Raw "special" milk.....	A	17.70	2.1
	B	17.08	2.1
Boiled "special" milk.....	A	17.24	2.2
	B	16.75	2.2
Evaporated (diluted with 1 part water; then diluted 2:1 as in other feedings)	A	18.73	2.2
	B	17.37	2.2
Dried milk (in "normal" dilution; then diluted 2:1 as in other feedings)	A	19.45	2.2
	B	21.03	2.2

* The dilution of two parts of milk to one part of water is used in this and in all subsequent tables unless otherwise stated.

Dilution with wheatena water was similar in effect to that with oatmeal water. The sodium chloride content in dextrimaltose number 1 did not noticeably affect the digestibility, but the effect of dextrimaltose number 3 must be discussed under alkaline additions, so markedly did the potassium bicarbonate influence the reaction.

The effect of fat in depressing the activity of pepsin was shown in digesting the Guernsey milk mixture. While the p_H was hardly changed, the digestibility fell almost to the level of that of the barley flour mixture.

Markedly low digestibility, showing the effect both of thickening with carbohydrates and of addition of fat in inhibiting peptic activity was shown when browned butter-flour mixture was added to the feedings. The digestion of the protein was only half that of simple cow's milk mixtures similarly diluted, though the p_H was little affected (table 4).

TABLE 3.—*The Effect of Addition of Carbohydrate on the Digestion of Milk by Pepsin*

Feeding	Sample	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Oatmeal water: 1 tb. : 500 cc. water (strained clear)	A	18.65	2.1
	B	17.44	2.1
Barley flour: 2-3 tb. : 250 cc. water (boiled thick)	A	12.94	1.9
	B	13.10	1.9
Banana: 1 tsp. mashed : 4 ounces milk	A	11.39	2.2
	B	11.05	2.2
Sucrose: 2 Gm. : 1 ounce milk	A	17.41	2.1
	B	17.56	2.1
Lactose: 2 Gm. : 1 ounce milk	A	14.04	2.1
	B	14.75	2.1
Dextrimaltose no. 2 (salt free): 2 Gm. : 1 ounce milk	A	17.79	2.1
	B	20.35	2.1

TABLE 4.—*The Effect of High Fat Milk and Addition of Butter-Flour Mixture and Gelatin on the Digestion of Milk by Pepsin*

Feeding	Sample	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Ordinary cow's milk mixture	A	18.53	2.1
	B	18.53	2.1
High fat milk mixture (Guernsey milk)	A	12.51	2.2
	B	15.73	2.2
Butter-flour addition	A	9.36	2.3
	B	9.36	2.3
Gelatin addition	A	10.57	2.3
	B	9.89	2.3

The effect of adding gelatin,[8] which produced a thick mixture, was to depress the peptic digestion both of the protein taken as a whole and of the milk protein taken separately. Gelatin has been added to feedings with a belief that it would aid rather than retard digestion, because of its acting as a protective colloid. The p_H of the mixture was slightly more alkaline, but the marked inhibiting effect was probably due to adsorption of the pepsin by the gelatin.

8. Downey, T. B.: The Nutritive Value of Gelatine, J. Metab. Research **5**:147, 1924.

Additions of egg yolk with or without lemon juice had no noticeable effect on digestibility or on the p_H.

The amounts of acid prescribed to produce a more acid, and therefore a more favorable p_H for peptic activity [9] (table 5) were found so small that, in the presence of as good a buffer as cow's milk, there was very slight or no change in the hydrogen ion concentration. Of course, at a more alkaline p_H range, there is a misleadingly greater numerical change on adding such amounts of acid, owing to the mathematical expression of the hydrogen ion concentration as p_H, in which the progression is logarithmic, not arithmetical, a change of 1 in one place at p_H 5 amounting to only 0.001 the grams of hydrogen ion which are expressed by a change of 1 in one place at p_H 2, at which hydrogen ion concentration pepsin is markedly active.

Of the acid additions studied (table 5), acetic acid, orange juice and tomato juice apparently somewhat inhibited peptic activity. Inhibition of peptic digestion by acetic acid was first found by Northrop.[10] Hess has reported the slightly unfavorable effect of lemon and orange juice, which he has attributed to a possible inhibition by the citrate ion. No inhibition was found, however, when citric acid was used in feedings.[11] As the juice of canned tomatoes was used for the tomato juice addition, it is difficult to suggest any reason for the low digestibility of the mixture.

As was to be expected, a marked or complete inhibition of peptic activity was observed when the alkalis, prescribed by some doctors [12] as additions to milk mixtures for infants, were incorporated in the feedings (table 6). It is of interest to note that addition of 2 grains (0.13 Gm.) of sodium citrate per ounce of milk produced a p_H of 2.7 in the digestion mixture, and that, nevertheless, 12.89 mg. of amino-nitrogen was

9. Faber, H. K.: Acidified Milks with Special Consideration of Indications and Limitations of Their Use, Am. J. Dis. Child. **31**:395 (March) 1926. Dunham, B. S.: Acetic Acid Milk from Acetic Acid of U. S. Pharmacopeia, Am. J. Dis. Child. **32**:384 (Sept.) 1926. Marriott, W. M., and Davidson, L. T.: Acidified Whole Milk as a Routine Infant Food, J. A. M. A. **81**:2007 (Dec. 15) 1923. Gonce, J. E., and Templeton, H. L.: Citric Acid Milk in Infant Feeding, Am. J. Dis. Child. **39**:265 (Feb.) 1930. Hess, Alfred A., and Matzner, Milton J.: Value of Milk Acidified with Lemon Juice, Its Combination with Egg Yolk to Add the Antirachitic Factor, J. A. M. A. **82**:1604 (May 17) 1924. Hess, J. H.: Feeding and the Nutritional Disorders of Infancy and Childhood, Philadelphia, F. A. Davis Company, 1927, pp. 165-169.

10. Northrop, J. H.: The Effect of Various Acids on the Digestion of Protein by Pepsin, J. Gen. Physiol. **1**:607, 1919.

11. Hess, J. H.: Feeding and the Nutritional Disorders of Infancy and Childhood, Philadelphia, F. A. Davis Company, 1927, p. 161.

12. Abt, Isaac A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 2, p. 654.

obtained per gram of protein, while with the addition of 1 grain (0.065 Gm.) of sodium bicarbonate per ounce of milk, complete inhibition of peptic activity resulted, with a digestion mixture more acid than with the sodium citrate addition, namely, p_H 2.4. The effect of adding 2 Gm. of dextrimaltose number 3 (containing potassium bicarbonate) per ounce of milk was like that of sodium carbonate. Lime water as used had the least inhibitory effect on peptic digestibility.

TABLE 5.—*The Effect of Additions of Acid on the Digestion of Milk by Pepsin*

Feeding	Sample	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Hydrochloric acid (0.1 N) 7.5 cc. : 1 oz. milk	A	17.83	1.9
	B	20.80	1.9
Lactic acid (U. S. P.) 0.2 cc. : 1 oz. milk	A	20.43	2.1
	B	21.70	2.1
Acetic acid (36%) 0.25 cc. : 1 oz. milk	A	16.53	2.1
	B	14.56	2.1
Citric acid, 0.125 Gm. : 1 oz. milk	A	17.80	2.0
	B	17.69	2.0
Lemon juice, 1 cc. : 1 oz. milk	A	17.60	2.1
	B	17.60	2.1
Orange juice, 2 cc. : 1 oz. milk	A	14.66	2.2
	B	15.40	2.2
Tomato juice, 3 cc. : 1 oz. milk	A	16.21	2.2
	B	14.19	2.2

TABLE 6.—*The Effect of the Addition of Alkalis on the Digestion of Milk by Pepsin*

Feeding	Sample	Gm. of Protein per Fluid Ounce of 30 Cc.	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Sodium bicarbonate, 1 grain (0.065 Gm.) : 1 oz. milk	A	0.663	0.00	2.4
	B	0.662	0.00	2.4
Sodium citrate, 2 grains (0.065 Gm.) : 1 oz. milk	A	0.661	12.89	2.7
	B	0.663	12.89	2.7
Lime water, 1.5 cc. : 1 oz. milk	A	0.647	12.81	2.2
	B	0.649	15.63	2.2

A few simple experiments were carried out to determine the rôle that the buffer action of the sodium citrate salts played in permitting digestion to take place as compared to complete inhibition of peptic digestion in bicarbonate mixtures.

On reversing the order of mixing and on adding the hydrochloric acid to the mixture before adding the pepsin solution, peptic digestion was, as expected, not inhibited by the bicarbonates, which showed that the destruction of the pepsin was due to the alkalinity produced before acidification. Next the p_H of the milk-alkali-pepsin mixtures was taken in

order to find out the difference in p_H between citrate mixtures and bicarbonate mixtures before and after the addition of the hydrochloric acid. It was found that the milk-bicarbonate-pepsin mixture was alkaline well into the destructive range for pepsin [13] before the hydrochloric acid was added, while the milk-citrate-pepsin mixture before the addition of the hydrochloric acid had a much more favorable, that is, more acid, p_H than the bicarbonate mixture. Further, the excellent buffer properties of the citrate salt controlled the p_H so that the final mixture of the citrate mixtures had a hydrogen ion concentration somewhat less acid than that of the bicarbonate mixtures, producing neutralization of the acid without the intermediate destructive effect on the enzyme of marked alkalinity, as was produced by the addition of sodium bicarbonate.

Alkalis then, unless previously acidified, inhibit digestion by pepsin because of destruction of the enzyme. As the feedings are acidified

TABLE 7.—*The Effect of Altered Milk Protein on Digestion by Pepsin*

Feeding	Sample	Gm. of Protein per Fluid Ounce of 30 Cc.	Mg. Nitrogen Produced in Four Hour Digestion per Gm. of Protein	p_H of Digestion Mixture
Whey (undiluted)	A	0.935	5.73	1.9
	B	0.935	4.76	1.9
Protein milk (diluted as per directions, then 2 : 1)*	A	0.594	25.08	2.0
	B	0.594	25.47	2.0

* Protein, 3.25 per cent; lactose, 2 per cent; butter fat, 2.21 per cent; lactic acid, 0.50 per cent; ash, 0.25 per cent.

in the stomach, the stomach is forced to produce exceptionally large amounts of hydrochloric acid if peptic digestion is to take place when alkaline feedings are used. The desirability of this gastric forcing is, of course, questionable, especially in the infant.

A most striking, though expected, difference was found between mixtures which contained large amounts of casein, as compared with the mixtures which contained large amounts of lactalbumin, with a negligible amount of casein. Despite a much more favorable concentration of protein and a similar p_H, the milligrams of amino-nitrogen produced per gram of protein are only about one-fifth as great per gram of whey, with its high lactalbumin content, as from the protein milk in which the protein is largely casein, as shown in table 7.

The point is emphasized that the comparative digestion of the feedings has been considered from the very limited angle of peptic digestion alone, and that only marked differences in digestibility as determined should be taken into account. Certain marked differences in the peptic

13. Northrop, J. H.: J. Gen. Physiol. **5**:465, 1920.

digestibility, however, have been observed. Further, as digestibility depends much on peptic activity, the effect of feeding of a milk mixture in promoting or inhibiting digestion by pepsin is of great importance, and it would seem worse than useless to prescribe a feeding that impairs peptic activity unless there is a good reason for doing so.

On considering the findings, it would seem an unnecessary procedure from the point of view of peptic activity to spend much time on cow's milk modification other than simple dilution and additions to meet nutritional requirements, with the possible exception of a milk high in casein or additions of hydrochloric or lactic acid for pathologic cases.

Further work on the problem both in vitro and in vivo would be exceedingly desirable. If the order of mixing the digests simply would be reversed, results would differ, and a maximum peptic digestion would be secured for all types of feedings through acidification with hydrochloric acid before the pepsin is added. It may be argued that the infant's stomach has the capacity to secrete sufficiently large amounts of hydrochloric acid to insure such acidification, and consequently a possible hydrogen ion concentration for peptic activity despite the alkalinity or buffer content of the feeding. The healthfulness of such unnatural stimulation, however, may indeed be questioned.

CONCLUSIONS

1. The methods as used have been found satisfactory for observing comparatively, in vitro, gross differences in actual peptic digestibility, e. g., breakdown of peptone linkages in milk mixtures.

2. While dilution markedly increased the hydrogen ion concentration, it did not markedly affect the peptic digestibility. It is possible that the decrease in concentration of protein due to dilution offset the more acid p_H.

3. Heating the milk, with or without concentration of the milk, did not markedly affect either the p_H or the digestion by pepsin.

4. The carbohydrate additions, which definitely thickened the mixtures, definitely depressed peptic activity. Carbohydrate additions, in general, did not affect the p_H.

5. Increasing the fat content of milk depressed peptic digestibility, but did not affect the p_H.

6. Increasing the proportion of casein to lactalbumin markedly increased peptic digestibility, while increasing the proportion of lactalbumin to casein noticeably decreased the peptic digestibility.

7. Of the two foreign proteins added, egg yolk had no effect on peptic digestion or on the p_H, but gelatin, which noticeably thickened the mixture, markedly depressed the peptic digestibility and very slightly affected the p_H.

8. Acid additions in general, as advocated, were found to be too small to increase markedly either the hydrogen ion concentration, in the presence of a good buffer such as cow's milk, or the peptic digestibility.

9. Unless the mixtures were acidified before the pepsin was added, the addition of alkalis, as was to be expected, inhibited the peptic activity, markedly or completely, according to the amount of alkalinity.

10. Further work on the problem needs to be done both in vitro and in vivo.

Professor Helen Monsch, New York State College of Home Economics, and Professor James B. Sumner, Medical College, Cornell University, Ithaca, New York, provided laboratory space and materials.

VITAMIN A CONTENT OF MILK IRRADIATED BY VARIOUS CARBON ARCS

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Enhancement of the antirachitic and calcifying properties of milk by exposure to ultraviolet rays has raised the question as to whether or not there was a destruction of vitamin A. Data from various laboratories have been contradictory, but a review of such data shows that a wide difference in the technic of irradiation, particularly in reference to the period of exposure, was in all probability the cause of the conflicting evidence. For illustration, Titus and Hughes [1] reported the apparent destruction of vitamin A in milk after an irradiation period of several minutes, whereas Supplee and Dow [2] reported that there was no measurable destruction of vitamin A after an exposure period of only sixteen seconds, during which substantial antirachitic properties were imparted to the milk.

Further work on the irradiation of milk at this laboratory,[3] wherein the physical characteristics of the radiant energy have been correlated with the biologic and clinical results, has provided an incentive for further studies on the vitamin A content of irradiated and nonirradiated milk. It is our purpose in this article to present supplementary data bearing on the vitamin A content of milk experimentally irradiated under carefully controlled conditions.

EXPERIMENTAL DATA

The milk was irradiated in thin, flowing films in fluid form and subsequently desiccated by the Just process. Immediately after desiccation, the dry milk was hermetically sealed in inert gas. The fluid milk contained 1.2 per cent butter fat.

From the Research Laboratories of the Dry Milk Company.

1. Titus, R. W.; Hughes, J. S.; Henshaw, W. R., and Fitch, J. B.: Destruction of Vitamin "A" in Milk by Ultra-Violet Light, J. Indust. & Engin. Chem. **18**:843, 1926.

2. Supplee, G. C., and Dow, O. D.: Vitamin "A" Potency of Irradiated Milk, J. Biol. Chem. **75**:227, 1927.

3. (*a*) Supplee, G. C.; Dorcas, M. J., and Hess, A. F.: Irradiated Milk: The Energy Requirements for Antirachitic Activation, J. Biol. Chem. **94**:749, 1932. (*b*) Supplee, G. C.; Hanford, Z. M.; Dorcas, M. J., and Beck, H. H.: Irradiated Milk: The Amount of Vitamin "D" and Its Rate of Formation, J. Biol. Chem. **95**:687, 1932. (*c*) Supplee, G. C.; Bender, R. C., and Dorcas, M. J.: Irradiated Milk: The Amount of Energy Required to Prevent Rickets in Chickens, J. Biol. Chem. **97**:67, 1932.

The various lots of experimental milk were irradiated and otherwise handled with commercial equipment in lots of approximately 1,000 pounds (453.59 Kg.) each. The periods of exposure to the radiant energy varied from eight to forty-eight seconds. Therapeutic carbons of the flaming arc type were used, specifically, the therapeutic "C" carbon, the magnesium impregnated carbon and the Sunshine carbon. Further and more complete details pertaining to these samples of milk are given elsewhere.[4] White rats from our standardized stock colony when from 25 to 28 days old were placed in metal cages on wire screen bottoms. They received the following basal diet: vitamin A-free casein, eighteen parts; Steenbock's salt mixture no. 40,[5] four parts; agar agar, two parts; dry yeast, six parts; dextrin, seventy parts. This ration was irradiated in a thin layer for twenty minutes at a distance of 26 inches (65 cm.) from a mercury vapor lamp in order to assure an adequacy of the antirachitic factor during the experimental period. The appearance of ophthalmia, bloody exudate of the nose, loss of weight or other symptoms of deficiency in vitamin A were the criteria which determined the depletion of the

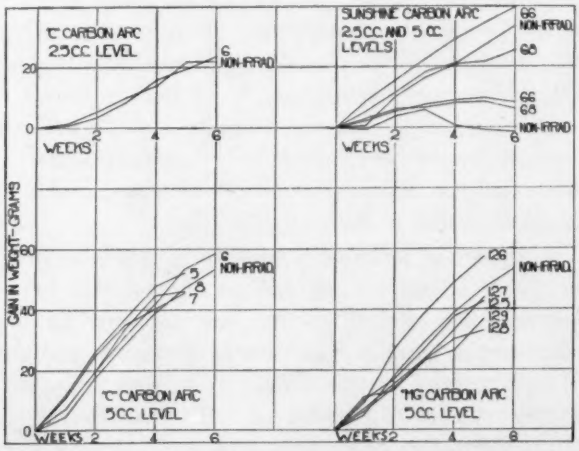

Chart showing vitamin A content of irradiated and nonirradiated dry milk. The curves indicate the average gain of rats during supplemental feeding of reconstituted dry milk as the only source of vitamin A. The numbers at the end of each curve represent milk sample numbers and correspond to sample numbers in accompanying table.

body reserve of vitamin A and the time at which the supplementary feeding of the reconstituted dry milk began. The samples of test milk were fed at levels of 2.5 and 5 cc. daily. The dry milk was reconstituted to the fluid form with the same concentration as the fluid milk from which it was prepared.

RESULTS

The results from these tests, which appear in the accompanying chart and table, were collected during a period of over a year, and

4. Supplee, Dorcas and Hess.[3a] Supplee, Hanford, Dorcas and Beck.[3b]

5. Steenbock, H., and Nelson, E. M.: Fat-Soluble Vitamine; Light in Its Relation to Ophthalmia and Growth, J. Biol. Chem. **56**:362, 1923.

Table Showing Comparative Vitamin A Potency of Reconstituted Dry Milk Irradicated by Different Carbon Arcs

Group	Sample	Arc	Exposure Period	Ergs per Cc. Milk ($\times 10^8$) 2,000-3,000 Angstrom Units	Number Rats		Highest Average Weight Before Change, Gm.		Average Weight at Change, Gm.		Number Rats with Ophthalmia		Time for Cure of Ophthalmia, Days		Number Rats with Abscesses at End of Experiment	
					2.5 Cc.	5 Cc.	2.5 Cc.	5 Cc.	2.5 Cc.	5 Cc.	2.5 Cc.	5 Cc.	2.5 Cc.	5 Cc.	2.5 Cc.	5Cc.
	X	Milk not irradiated.....	None	None	15	13	98	98	82	84	8	7	18	14	7	4
I-AC-60	5	"C" carbon.....	8	989	..	4	..	86	..	68	..	4	..	13	..	1
I-AC-60	6	"C" carbon.....	16	2,016	11	11	91	96	73	74	7	7	17	17	5	4
I-AC-60	7	"C" carbon.....	32	4,292	..	4	..	90	..	87	..	4	..	16	..	1
I-AC-60	8	"C" carbon.....	48	6,780	..	4	..	96	..	77	..	4	..	14	..	0
III-AMG-60	125	Magnesium carbon.....	8	796	..	4	..	87	..	69	..	4	..	16	..	1
III-AMG-60	126	Magnesium carbon.....	16	1,548	..	4	..	96	..	69	..	3	..	12	..	1
III-AMG-60	127	Magnesium carbon.....	32	3,124	..	4	..	97	..	76	..	3	..	17	..	0
III-AMG-60	128	Magnesium carbon.....	48	4,740	..	4	..	113	..	97	..	3	..	28	..	0
III-AMG-80	129	Magnesium carbon.....	8	1,225	..	4	..	113	..	85	..	2	..	18	..	2
	XX	Milk not irradiated.....	None	None	5	5	119	108	115	101	4	3	19	13	4	1
II-AS-60	66	Sunshine carbon.....	16	528	10	11	115	105	110	99	6	7	18	20	4	4
II-AS-60	68	Sunshine carbon.....	48	1,557	11	11	105	106	102	103	8	*6	18	18	2	5

each of the curves represents the average gain of from four to fifteen rats during the period of supplemental feeding following the depletion of the body reserve of vitamin A. Owing to the extended period over which the data were obtained, variations in the different lots of animals as well as other possible sources of variability have entered into the composite results recorded. However, such variations as may have prevailed at the different periods of assay are common to the experimental and the control groups. Therefore, it is believed that these results are representative of what may be expected in the commercial irradiation of similar milk treated under the same conditions.

The two levels of nonirradiated milk which serve as a basis for comparison in the Sunshine carbon arc group are directly comparable with the milks treated by this carbon and are, therefore, presented in a group by themselves, as will be observed in the chart. The differences observed between the results from this experimental group and the results from the other groups are no doubt due for the most part to variations in the vitamin A content of the original milk.

The data for both the 2.5 and the 5 cc. levels of feeding seem to indicate that there is practically no difference in the vitamin A content of the milk before and after irradiation by any of the various sources of light used. There appears to be no significant reduction in the vitamin A content of the irradiated milk exposed for as long as forty-eight seconds, during which as much as 6,780,000 ergs (from 2,000 to 3,000 angstroms) were applied to each cubic centimeter of milk.

SUMMARY

Data are presented which indicate that there is no significant destruction of vitamin A in milk containing 1.2 per cent butter fat resulting from direct irradiation with different carbon arcs for periods varying from eight to forty-eight seconds under the conditions herein described.

BLOOD GROUPING

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A few years ago a transfusion service was organized at the Milwaukee Children's Hospital by one of us (S. J. S.) of the surgical staff. Before that time transfusions were done by the resident physician or the interns, and often the only record of the operation was a terse statement on the hospital chart that the transfusion had been made. Since we took over the service, one man has been responsible for all of the transfusions performed on patients in the hospital, and accurate records have been kept. Necessarily a great many blood groupings and compatibility tests have been made preliminary to the transfusions. It occurred to us that a study of this material might be of value, not only in giving us a better understanding of the fundamental principles involved, but also as a contribution to the studies of hereditary and forensic problems that are being discussed in the present-day literature on the subject. Even the laity has been introduced to "blood tests" for the determination of parentage of children by vague references in the daily press.

The vast amount of literature on the subject of blood grouping is mute evidence of the tireless efforts of many persons to untangle the behavior of the four blood groups, which most physicians take as a matter of fact, and the determination of which is allowed to become a mere routine to establish the compatibility of donor's and recipient's blood.

Although isohemagglutination was probably observed by Maragliano [1] in 1892 and Shattock [2] in 1899, the first definite statement of its occurrence was made by Landsteiner [3] in February, 1900. The early writers on this subject thought that hemagglutination was in some way linked with disease processes, and many pages have been written on the agglutinating property of serums in various diseases. This was probably a reflection of the works of Ehrlich, which were constantly appearing in the literature of the period. This type of work is still being

1. Maragliano, E.: Contribution to the Pathology of the Blood, Verhandl. d. Cong. f. inn. Med. **11**:152, 1892.

2. Shattock, S. G.: Chromocyte Clumping in Acute Pneumonia and Certain Other Diseases and the Significance of the Buffy Coat in the Shed Blood, Tr. Path. Soc., London **50**:279, 1899.

3. Landsteiner, K.: Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe, Centralbl. f. Bakt. (Abt. 1) **27**:357 (Feb.) 1900.

carried on, but with a different point of view—that of establishing whether or not there is a linkage of the factors in blood groups with those of immunologic states. Halban,[4] in 1900, working with the blood of mothers and their new-born infants, recognized hemagglutination as a normal occurrence, but made no attempt to formulate definite groups. In 1901 Landsteiner [5] grouped twenty-two persons and divided them into groups A, B, and C. One year later, de Castello and Sturli [6] added a fourth group, but did not designate it as such. Hektoen,[7] in 1907, also noted blood which did not belong in groups A, B or C of Landsteiner. In 1907, Jansky [8] reported the four groups which are a matter of common knowledge today. Jansky's paper is not generally available, but recently Kennedy [9] has given us a critical analysis of Jansky's work, which should be read by every one interested in the subject if he is to appreciate the magnitude of Jansky's labors. Independently and without knowledge of Jansky's publication, Moss,[10] in 1910, reported similar findings, but his groups one and four were the reverse of Jansky's. More recently Guthrie and Huck [11] have shown that group two can be divided into two subgroups, but practically this has only limited significance. There are three classifications now in common use, which makes for some confusion; the newer international nomenclature, as recognized by the Health Committee of the League of Nations, should be the one generally adopted.

Jansky	Moss	International
I	IV	O
II	II	A
III	III	B
IV	I	AB

It was only a short time after the phenomenon of hemagglutination was observed that writers began to theorize on the mechanisms involved

4. Halban, J.: Agglutination Experiments with Blood of Mother and Child, Wien. klin. Wchnschr. **13**:545, 1900.

5. Landsteiner, K.: Ueber Agglutinationserscheinung normalen menschlichen Blutes, Wien. klin. Wchnschr. **14**:1132, 1901.

6. de Castello, A., and Sturli, A.: Ueber die Isoagglutinine im Serum gesunder und kranken Menschen, München. med. Wchnschr. **49**:1090, 1902.

7. Hektoen, L.: Isoagglutination of Human Corpuscles with Respect to Demonstration of Opsonic Index and to Transfusion of Blood, J. A. M. A. **48**: 1739 (May 25) 1907.

8. Jansky, J.: Hämatologische Studie und Psychose, Sborn. Klin. v. Praze **8**:85, 1906-1907.

9. Kennedy, James A.: Isohemagglutination: The Work of Jan Jansky, with a Critical Analysis, J. Immunol. **20**:117 (Feb.) 1931.

10. Moss, W. L.: Studies on Isoagglutinins and Isohemolysins, Bull. Johns Hopkins Hosp. **21**:63 (March) 1910.

11. Guthrie, C. G., and Huck, J. G.: On the Existence of More Than Four Isoagglutinin Groups in Human Blood, Bull. Johns Hopkins Hosp. **34**:37, 1923.

in the process. Thus Halban,[4] in 1900, applying the conception of Ehrlich to agglutinins, assumed that there were congenital agglutinins, which he termed "iso-agglutinins," and acquired agglutinins, or "idio-iso-agglutinins," and the corresponding lysins, or "idio-iso-lysins." The lysins were probably due to the constant destruction of red cells in the circulation, and the agglutinins to congenital properties in the blood. Eisenberg [12] also believed that the iso-agglutinins and isolysins were an expression of the reaction of the organism to an absorption of erythrocytes or their components. Halban [4] and, later, Halban and Landsteiner [13] determined that mother and child react differently to a given serum or cells, and they regarded new-born infants as not fully developed in respect to their agglutinating power. De Castello and Sturli [6] came to the conclusion that children under 6 months of age showed deviations from the typical reaction because secondary immunization had not taken place, although primary agglutinins were present. They also stated that rouleux formation had nothing to do with agglutination. Unger,[14] in 1921, stated that children do not acquire receptors in their cells until they are 6 months old, and the agglutinins in the serum until they are from 2 to 4 years old. De Biasi,[15] in 1923, reported good evidence to show that infants do have their full quota of receptors at birth.

In attempting to explain the existence of four blood groups, Moss assumed that there were three agglutinins, one for each of the groups two, three and four of his classification. Von Dungern and Hirschfeld [16] concluded, however, that the specific structures of the blood were inherited according to Mendel's law, the agglutinogens acting as dominants and the lack of them as recessives. It was soon found, however, that the heredity of the blood groups could not be explained on the basis of two independent pairs of genes, and Bernstein [17] in 1925, sub-

12. Eisenberg, P.: Isoagglutinins and Isolysins in the Human Sera, Wien. med. Wchnschr. **14**:1020, 1901.

13. Halban, J., and Landsteiner, K.: Ueber Unterschilde des fötalen und mutterlichen Blutserums und über eine agglutinations und follungshemmende Wirkung des Normalserums, München. med. Wchnschr. **49**:473 (March 25) 1902.

14. Unger, Lester J.: Precautions Necessary in the Selection of Donor for Blood Transfusion, J. A. M. A. **65**:9 (Jan. 1) 1921.

15. de Biasi, Bruno: Studies on Isoagglutinins in the Blood of the New-Born, J. A. M. A. **81**:1776 (Nov. 24) 1923.

16. von Dungern, E., and Hirschfeld, L.: (*a*) Hereditary Transmission of Group Specific Structures of the Blood, Ztschr. f. Immunitätsforsch. u. exper. Therap. **6**:284, 1910; (*b*) Demonstration and Inheritance of Biochemic Structure, ibid. **4**:531, 1909-1910; (*c*) Ueber gruppenspezifische Strukturen des Blutes, ibid. **8**:526, 1910-1911.

17. Bernstein, F.: Zusammenfassende Betrachtungen über die erblichen Blutstrukturen des Menschen, Ztschr. f. indukt. Abstammungs. u. Vererbungal. **37**: 237, 1925.

stituted the conception of three multiple allelomorphs. Furuhata,[18] during the same year, formulated a hypothesis much like Bernstein's, except that he took into consideration factors in the serum as well as in the cells. In 1926 he changed his hypothesis somewhat in regard to the factors in the serum. Both he and Bernstein, however, came to the same conclusion in their formula for heredity. Further careful work is necessary to prove whether the serums of all of the groups are alike, as Bernstein contended, or whether the factors in the serums differ, as Furuhata proposed. Bauer[19] attempted to explain the heredity and distribution of the blood groups on the basis of linkage with some crossing over, but it is now generally held that this is not tenable, because the calculated value for crossing over would be 10^{-7}, which would make the observations of such crossings over highly improbable, and this is not in accordance with the facts.

Von Dungern and Hirschfeld[16a] assumed that there are two agglutinogens and two agglutinins, the former in the cells and the latter in the serum. The agglutinogens are inherited as mendelian dominants. Thus von Dungern and Hirschfeld formulated the first theory, which is generally believed to be correct, that a child cannot have an agglutinogen unless one of the parents possesses the same factor. In their hypothesis they further assume that the absence of a specific agglutinin is possible only in the presence of its corresponding agglutinogen.

Bernstein, in his hypothesis, assumes that the serums of all four groups are identical, and that there are really three factors in the cells and the serum. He believes that there has been a mixture of three races, which he designates as A, B and R races. By mathematicostatistical methods he is able to compute the numerical percentage law of each of the three races any place on earth. It must be assumed that A race and B race are mutations, and apparently late mutations, of the R race. The R race is represented relatively purely by the Filipinos; the B race can apparently be localized in Central Asia, probably the Turkish population; the A gene is less definite, but probably can also be traced to Central Asia. On the basis of these three multiple allelomorphs, a theoretical scheme can be constructed which fulfils nearly all of our observations up to the present on the behavior of blood groups.

Furuhata recognized only two factors in both the cells and the serum. His group O is characterized by the lack of specific group agglutinogens; therein he differs from Bernstein, who assumes in his hypothesis that there is a specific group agglutination of group O cells. He is supported by Schiff, while Uemichi and others in Furuhata's labo-

18. Furuhata, T.: A Summarized Review of the Gene-Hypothesis of the Blood Groups, Am. J. Phys. Anthropol. **13**:109 (April-June) 1929.

19. Bauer, K. H.: Zur Lösung des Problems der Blutgruppenvererbung, Klin. Wchnschr. **7**:1588 (Aug. 19) 1928.

ratory cannot confirm this assertion. Furuhata's hypothesis differs from that of Dungern and Hirschfeld in that the latter assume four genotypes in group AB, while he and Bernstein assumed only one genotype in group AB.

TABLE 1.—*Comparisons of the Genotypes in the Three Hypotheses*

Phenotype	Dungern and Hirschfeld	Bernstein	Furuhata
O	a a b b	R R	a b a b
A	A A A a b b b b	A A A R	A b A b A b a b
B	B B B b a a a a	B B B R	a B a B a B a b
AB	A A A a A A A a B B B B B b B b	A B	A b a B

TABLE 2.—*Distribution of Parents*

	Number	Percentage
Group O	206	42.13
Group A	177	36.19
Group B	68	13.90
Group AB	38	7.78

TABLE 3.—*Various Matings and the Children from Each Crossing*

Father	Mother	Child O	Child A	Child B	Child AB	Total
O	O	34	1			35
O	A	17	8	1	1	27
O	B	5		5		10
O	AB		3			3
A	O	19	16			35
A	A	6	14	1		21
A	B		1	1	3	5
A	AB		3	5	2	10
B	O	3		7		10
B	A	2	4	3	2	11
B	B	1		3		4
B	AB	.....	.....	.....	.....	0
AB	O	1	3	2		6
AB	A		1	2	3	6
AB	B				1	1
AB	AB	1			3	4

Table 1 gives a comparison of the genotypes in the three hypotheses; the capital letters represent the factors in the cells, and the small letters the factors in the serum.

Bernstein's is the most widely accepted hypothesis at the present time.

We have the complete records of 489 patients who were grouped for transfusion in the past three years. Frequently both the mother and the father were grouped to act as donors. Most of the groupings were

done by the technicians at the Milwaukee Children's Hospital, some at other hospitals and some by one of us (A. A. S.). Although we use the Moss classification for reporting blood groups in our daily routine, the international classification will be used throughout this paper. The distribution of the patients in the various groups is given in table 3.

The mother, father and child were grouped in 188 instances; the father and child in 126, and the mother and child in 112. In the remaining cases, neither the father nor the mother was grouped, the donors being relatives, friends or professional donors. Table 3 gives the various matings as they occurred, and the number of children in the groups found from each crossing.

Table 4 gives the number of children of fathers in the various groups, and table 5 the offspring of mothers in all the blood groups.

TABLE 4.—*Offspring of Fathers in Each Group*

	Child				
Father	O	A	B	AB	Total
O	42	6	5	1	54
A	5	50	2		57
B	2		7		9
AB	1			5	6

TABLE 5.—*Offspring of the Mothers in Each Group*

	Child				
Mother	O	A	B	AB	Total
O	52	6	1		59
A	5	28			33
B	1	1	10		12
AB				8	8

On examination of table 3 we find that there are four different matings yielding offspring not to be expected with any existing hypothesis. These matings, the first group representing the father, the second the mother and the third the child, are as follows:

O × A — AB
O × A — B
O × O — A
A × A — B

In the first case the child had been grouped as an O on a previous occasion; this, the second grouping, is therefore very likely due to an error made in the laboratory. The father was used as the donor in the case. In the second case, although the laboratory reported the father as belonging to group A and the child as belonging to group B, the cross-matching showed no agglutination. Obviously, this, too, must be due to an error in the laboratory. The father was used as donor. No reaction followed either of these transfusions. And if we are to believe

in any hypothesis of the heredity of blood group factors, we must charge the last two combinations to technical error, as they cannot be explained by any hypothesis, except that both of these children are illegitimate. Thus far, with the exception of the four cases cited, all of the cases can be explained by the hypothesis of independent pairs or genes.

Matings which involve group AB are the best tests to determine the validity of Bernstein's hypothesis of a triple allelomorph, because if it is true, the crossing of a group AB with any other group cannot result in a group O, or if the child is a group AB, neither the father nor the mother can be a group O. Crossing a group O with an AB is an especially good test, because the offspring can be in only group A or B. In table 3 are thirty cases which involve group AB. There are nine O × AB matings, sixteen A × AB, one B × AB and four AB × AB matings. Two of these, O × AB—O and AB × AB—O, do not uphold the theory of a triple allelomorph. No effort has been made to determine whether or not there is any possibility that these offspring might be illegitimate. In table 4 there are an additional fifteen cases which involve group AB, and among these are two instances, O × ?—AB, and AB × ?—O, which do not uphold the hypothesis of a triple allelomorph. There are no exceptions to the hypothesis in table 5. This leaves a total of four cases which cannot be explained by the hypothesis of Bernstein. This does not seem such a large figure when there are so many sources of error. There is a slight possibility that some of these offspring may have been from a previous marriage, as two such instances were found in checking our records. The question of illegitimacy is difficult of approach in this class of patients and has not been attempted in this series. As was intimated before, probably the greatest number of errors arise through technical mistakes in the laboratory. Most of the exceptions noted occurred in the older records, when the laboratory staff was probably not as efficient in the technic of blood grouping as it now is.

COMMENT

Since the forensic aspect of this problem has become so important in recent years, and since the mass statistics of blood groups have great value in anthropologic studies, it might be well for all laboratories making a great many blood groupings to gather their data a little more carefully, and with an attempt to eliminate as much as possible the errors inherent in the casual methods now employed. An active interest in a subject of this sort adds an additional check to laboratory methods, because when an exception to one or the other hypothesis is found, the blood groupings should be repeated.

The value of blood groups in the determination of paternity is becoming an important development, as evinced by the studies of

Buchanan, Mayser, Haselhorst, Meixter, Thomsen, Weiner, and Landsteiner and Levine. The latter authors have found additional specific agglutinins (M and N) in normal human serum by means of immune rabbit serum. These agglutinins are also inherited, according to Mendel's law, and may be a further means of detecting parentage in doubtful cases.

Anthropologic studies are being carried on mostly by Bernstein and Snyder. An excellent review of the results was made by Snyder,[20] who compiled all of the statistics up to 1926.

CONCLUSIONS

1. Of the 489 patients grouped for transfusion, 42.13 per cent were in group O; 36.19 per cent in group A; 13.90 per cent in group B, and 7.78 per cent in group AB.

2. The groups of mother, father and offspring are given in 188 cases; the father and child in 126, and the mother and child in 112.

3. Four matings yielded offspring which cannot be explained by any existing hypothesis.

4. Four matings were not valid according to the triple allelomorph hypothesis, but are compatible with the hypothesis of two independent pairs of genes.

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20. Snyder, L. H.: Human Blood Groups: Their Inheritance and Racial Significance, Am. J. Phys. Anthropol. **9**:233, 1926.

INTERPLAY OF PIESTIC FACTORS AT BIRTH

WITH A CONSIDERATION OF THEIR PHYSIOLOGIC AND CLINICAL SIGNIFICANCE

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In reviewing the factors concerned with the function of the ductus arteriosus, a hypothesis of the interplay of piestic factors at birth has been developed which coordinates the data of all the previous antagonistic theories dealing with this process. The major tenets have been held and tested over a period of two years. Recently, while reviewing the bibliographic references to the subject, my associates and I came across the theory of "reversal" of the respiratory center as developed by Schmidt.[1] This concept fits so perfectly into our argument that we believe our hypothesis supported in every detail and hence venture this initial report, since we think that the interpretation of asphyxia neonatorum and cerebral hemorrhage in the new-born is materially advanced.

In presenting our experimental and observational data, we shall not follow the typical form of organization, but shall introduce the materials at the points where they fit most logically into the argument.

CURRENT CONCEPT

The current concept of circulatory changes at birth as given in the majority of textbooks of embryology, obstetrics and pediatrics is as follows. Parturition leads to placental interference and a subsequent increase in the carbon dioxide concentration in the blood of the newborn. This increase acts as a respiratory stimulus, and respiration is started. With inflation of the lungs, the collapsed, "tortuous," pulmonary vascular bed is opened, and the flow from the right ventricle, previously passing by way of the ductus arteriosus to the descending aorta, is diverted through the pulmonary arteries. The return of this voluminous flow to the left atrium increases the pressure locally, and the foramen ovale is closed. The left ventricle is now called on to maintain the flow through the systemic aorta and placenta. The resulting fall in pressure leads to a passive collapse of the umbilical circulation,

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1. Schmidt, C. F.: Am. J. Physiol. **84**:202, 1928.

both arterial and venous, with a subsequent obliteration of the hypogastrics, ductus venosus and ductus arteriosus.

The observed facts which have been brought against this explanation are so numerous and diverse that the theory is no longer tenable. Scammon and Morris [2] have shown statistically that only 0.7 per cent of cases show a closure of the foramen ovale in the first eight days post partum, while the values for the ductus arteriosus are 0.3 per cent and for the ductus venosus, 2.3 per cent. Patten [3] has shown anatomically that these fetal channels are not abandoned at once. Dunn [4] questioned the theory of early abandonment on clinical grounds and further stated that autopsy gives incorrect data as to the frequency of patency.

There is also a wide diversity of opinion as to the chronology of events and their causal relationships. Thus, respiratory reflexes are known to occur in utero (Ahlfeld [5]). Again, they quite commonly occur during the passage through the birth canal long before any interference with the placental circulation could be postulated. Pulsation in the cord may cease before respiration is started, or, again, it may be delayed for fifteen minutes after birth (Franklin [6]). Cessation of pulsation in the cord is considered to be due to circulatory failure, yet the pulsations do not correspond grossly with the fetal pulse, but give the impression of an active spasm.

In the initial theory, the peripheral resistance in the pulmonary bed is considered to be removed by the act of breathing. There is no agreement, however, on the part of investigators as to the effect of inspiration on relieving the peripheral resistance in the adult lung even after the circlation is well established. These facts were reviewed by Blumgardt,[7] Daly [8] and many others. Thus, Andrus [9] has shown evidence of a marked circulation through the collapsed lung after ligation of the primary bronchus.

Furthermore, Coryllos [10] claimed that the lung is inflated more during expiration than inspiration, a factor which would tend to increase and maintain peripheral resistance rather than to relieve it.

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2. Scammon, R. E., and Morris, E. H.: Anat. Rec. **15**:165, 1918.

3. Patten, B. M.: Am. J. Anat. **48**:19, 1931.

4. Dunn, C. H., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 3, p. 13.

5. Ahlfeld, F.: Lehrbuch der Geburtshilfe zur wissenschaftlichen und praktischen Ausbildung für Aerzte und Studierende, Leipzig, F. W. Grunow, 1903.

6. Franklin, M.: Am. J. Obst. & Gynec. **22**:913, 1931.

7. Blumgardt, H. L.: Medicine **10**:1, 1931.

8. Daly, I. de B.: J. Physiol. **69**:239, 1930.

9. Andrus, W. DeW.: Observations on the Cardiorespiratory Physiology Following the Collapse of One Lung by Bronchial Ligation, Arch. Surg. **10**:506 (Jan.) 1925.

10. Coryllos, P. N.: Am. J. Obst. & Gynec. **21**:512, 1931.

Stewart [11] has restudied the changes in the lung immediately before and at the time of birth, and from an examination of his figures it is difficult to discover a mechanism producing "peripheral resistance," which is relieved with inspiration.

We have attempted to check two of the foregoing points by the production of a unilateral pneumothorax in a kitten as it passed the birth canal before the first breath was taken. The two lungs were fixed on the subsequent day and examined histologically. The changes in the respiratory epithelium described by Stewart were markedly in evidence, and the atelectatic lung showed marked evidence of a profuse flow.

In certain of the variations of the initial theory, the collapse of the umbilical circulation is considered to be dependent on a pressure reversal in the pulmonary and systemic circuits at birth. Abbott [12] assumed a very high pulmonary pressure before birth. Wells [13] considered the pressure in the pulmonary circuit to be three times that in the aorta, with a reversal of relationships with the establishment of the pulmonary flow, resulting in the collapse of the ductus arteriosus. These views were developed in an attempt to account for the closure of the ductus arteriosus. Pohlman [14] and Kellogg [15] have shown by direct measurement, however, that the pressures in the right and left ventricles are equal; their capacities are equal, and their myocardia are equally developed. Since the aortic and pulmonary trunks are equal in size and are connected by a competent shunt, their pressures likewise are equal.

In Wiggers' [16] discussion of the changes in circulation at birth, a drop in both the pulmonary and the systemic pressure is assumed. A carbon dioxide increase, due to placental interference, gives a vigorous ventricular output and a temporary pressure elevation which forces the pulmonary bed. With the establishment of the pulmonary circuit, the pulmonary pressure drops. The backflow through the ductus arteriosus causes a drop in the aortic pressure as well, and since the aortic supply is derived from the left ventricle only, a further drop in pressure is accomplished with a complete failure of the umbilical circulation. Wiggers premises his drop in pressure on the basis of an observed acceleration of the heart rate, which is interpreted as an effort to compensate. If this explanation were correct, there should be a decrease

11. Stewart, F. W.: Anat. Rec. **25**:181, 1923.

12. Abbott, M. E.: Congenital Cardiac Diseases, in Osler, William, and McCrae, Thomas: Modern Medicine, Its Theory and Practice, Philadelphia, Lea & Febiger, 1915.

13. Wells, H. G.: Am. J. M. Sc. **136**:381, 1908.

14. Pohlman, A.: Anat. Rec. **13**:1, 1909.

15. Kellogg, H. B.: Am. J. Physiol. **91**:637, 1929.

16. Wiggers, C. J., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 4, p. 198.

in the rate as soon as the umbilical load were removed, that is, with the cessation of pulsation in the cord. This is not the case, however, since the rate is maintained at the high level of 170 for from fifteen to thirty minutes after birth.

To account for the voluminous flow through the lungs sufficient to bring about these marked pressure relationships, it would be necessary to assume a complete opening of the pulmonary bed, yet von Reuss (cited by Seham [17]) has shown that the alveolar capacity at the end of twenty minutes is only 17 cc.; at three and one-half hours, 21 cc., and at six hours, 36 cc. Wasson,[18] studying this problem with the x-rays, has shown that complete inflation is never accomplished under five minutes, and that it may require as much as three weeks. Seham [17] stated further that two thirds of the lung may remain atelectatic without distress.

NATURE OF RESPIRATORY STIMULUS

If the foregoing considerations of pressure were correct and the chronology and causal relations were established, one most perplexing point would still exist without explanation. Eastman [19] closed a recent article with the following statements: "The exact cause of the onset of respiration at birth, as well as the nature of the intra-uterine apnea, remains obscure. The relatively high carbon-dioxide tension of the fetal blood as it exists in utero, seems difficult to reconcile with a state of apnea, and at present this phenomenon can only be explained by assuming that the sensitivity of the fetal respiratory center, in respect to this gas at least, is markedly depressed." In view of the careful work by Eastman on carbon dioxide tension, oxygen tension, lactic acid concentration and p_H of the fetal blood, this admission is significant.

It is common knowledge that obstetric practice varies widely in its methods of resuscitation, based on the variety of concepts of the nature of the initial respiratory stimulus. Spanking, ice-water baptism, compression, mouth to mouth breathing, inhalation of carbon dioxide and oxygen, caffeine, alpha-lobeline and a host of other stimulants have been tried without universal success and more frequently with deplorable results. Ahlfeld [5] has shown that cold is nonessential. Huggett [20] has evaluated stimulation of the skin, sciatic reflexes, vagus reflexes, intratracheal pressures and decapitation in fetal goats and has shown that the respiratory center is developed and subject to strong stimulation even from four to six weeks before term.

17. Seham, M., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 4, p. 239.

18. Wasson, W. W.: A Roentgenographic Study of the Infant Chest as Seen at Birth, J. A. M. A. **83**:1240 (Oct. 18) 1924.

19. Eastman, N. J.: Bull. Johns Hopkins Hosp. **50**:39, 1932.

20. Huggett, A. St. G.: J. Physiol. **69**:144, 1930.

In cases in which the application of the routine methods of resuscitation has failed, it is generally assumed that some interference has taken place in the placental circulation with asphyxia in utero. It is even assumed that eight minutes constitute the period after which resuscitation is hopeless. We wish to point out here, however, that placental interference during the contraction of the uterus in delivery is not proved. As a matter of fact, the condition existing in the delivery of monochorionic twins demands the maintenance of a functioning placenta far beyond the eight minute period. Otherwise, the carbon dioxide concentration sufficient to constitute a respiratory stimulus in the first twin would, through their common circulation, induce respiration in the second twin, and suffocation would always result before it could engage and be delivered.

This criticism also holds for any other interpretation of the nature of the respiratory stimulus, such as carbon dioxide, oxygen, p_H, lactic acid concentration or hormone, which does not at the same time premise an obliteration of the umbilical circulation concomitant with delivery.

From the foregoing facts, it becomes apparent that the problem of the initiation of respiration and circulatory adaptation at birth as it is commonly presented is far from satisfactory. There are, however, certain considerations of the changes in pressure, when combined with the theory of "reversal," which provide a mechanism making the entire process rational. These two concepts and their interrelation will now be presented.

Gesell [21] and Schmidt [1] have reviewed the newer concepts of respiratory control in the adult. Schmidt has shown experimentally that three factors are primarily concerned: (1) concentration of material (carbon dioxide) in the arterial blood, (2) the rate at which the stimulant (carbon dioxide) is produced in the respiratory center and (3) the rate of the blood flow through the center. Cerebral anemia, produced either by clamping the carotid and vertebral arteries or by temporarily stopping the perfusion pump, is followed first by dyspnea and later by hyperpnea and respiratory failure. If the clamps are removed during the dyspneic period, apnea follows associated with the period of return of the blood to the center. This condition is designated as the "reversal" and is explained as an abnormal state of irritability of the center produced by a decreased blood supply and general anoxemia. In this condition, a normal stimulus, such as carbon dioxide, may cause further depression.

The low threshold of stimulation of the respiratory center during intra-uterine life suggests that the physiologic state of "reversal" exists. Eastman [19] has shown that the carbon dioxide tension in the fetal blood is always higher than that in the maternal venous blood, and yet apnea

21. Gesell, R.: Physiol. Rev. **5**:551, 1925.

persists. Hence, any factor that increases the cerebral flow may shift the threshold of stimulation and initiate respiration. An evaluation of the interplay of piestic factors at birth may now be undertaken.

PIESTIC FACTORS AT BIRTH

Most attempts to explain circulatory adaptation at birth have dealt only with pressures. We have adopted the term piestic factors to signify not only pressures, but load, force and resistance. We justify the use of the term on the basis of precedent of Allbutt's hyperpiesia.

The load of the heart in utero consists in maintaining both the systemic and the placental flow. The total blood volume in the fetus and the placenta has been variously estimated at from 250 to 350 cc. (Abt [22]). On the basis of 8.8 per cent of total body weight, Wiggers [16] calculated the blood volume of a 3 Kg. fetus to be 264 cc. Lucas and Dearing [23] have shown a variation of blood volume in the new-born ranging from 10.7 to 19.5 per cent, with an average of 14.7 per cent. Schloss and Crawford [24] cited an old observation by Hofmeir (1897), that from 38 to 100 cc. of blood may be added to the fetal circulation by late ligation. We have drained approximately 120 cc. of blood from the severed umbilical cord during the delivery of the placenta. For purposes of comparison the total load may then be taken at 350 cc., with 100 cc. in the placenta.

The force necessary to move this load is developed by the combined action of the right and left ventricles acting through the pulmonary and aortic trunks. That this load is practically equally divided is shown by the equal development of the myocardium and by equal pressures, equal capacities and equal outlets (Pohlman [14] and Kellogg [15]). The magnitude of the load is shown by the fact that the heart is at its greatest proportional development at the time of birth, constituting 0.86 per cent of the total body weight, as compared to 0.52 per cent in the adult (Seham [17]).

At birth the placental circulation is obliterated and the total load is reduced 100 cc. This load now falls practically entirely on the left side of the heart, except for the small portion diverted to the pulmonary circuit, the maintenance of which is now the function of the right side of the heart.

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22. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923.

23. Lucas, W. P., and Dearing, B. F.: Blood Volume in Infants Estimated by the Vital Dye Method, Am. J. Dis. Child. **21**:96 (Jan.) 1921.

24. Schloss, O. M., and Crawford, J. L.: The Metabolism of Nitrogen, Phosphorus and the Purin Substances in the New-Born, With Special Reference to the Causation of the Uric Acid Infarcts of the Kidney, Am. J. Dis. Child. **1**:203 (Jan.) 1911.

In order to check the relative distribution of the load in utero and the shift at birth, we made estimates of the distribution of blood in the placenta, the fetal systemic circuit and the fetal lungs. Fetal pigs were used as material because the entire membranes may be shelled out of the uterus without loss of blood or contamination from a maternal source. The sacs were opened, and the cords were tied with double ligature and severed. The lungs were removed by section between the double ligature at the base of each. The separated membranes, lungs and fetuses were then macerated in a mill, and equal volumes of 10 per cent hydrochloric acid were added to each and allowed to stand for thirty minutes. The color was then checked against a standard solution made by treating 1 cc. of blood with 10 cc. of hydrochloric acid and diluting

Hemoglobin Content of Placentas, Lungs and Bodies of Fetal Pigs

Animal Number	Grams of Hemoglobin in			Total
	Lungs	Bodies	Placentas	
1, litter 1	3.50	....	53.0	
2, litter 1	....	87.5	....	
3, litter 1	....	65.5	34.3	
4, litter 1	....	75.6	47.5	
5, litter 1	....	58.5	48.3	
6, litter 2	4.11*	....	53.7*	
Average, Gm.	3.83	71.6	47.3	122.73
Average percentage of total	3.11	58.39	38.50	
Human fetus, 260 mm., stillborn	2.127	25.95	11.79	39.63
Percentage of total	5.31	65.19	29.50	

* Average for five pairs of lungs of the second litter; only one placenta was tested for this litter.

to 100 cc. The hemoglobin content of the blood had been previously estimated by comparison with a standard Sahli in the regular manner.

The labor involved and the scarcity of material limited the number of tests. One stillborn human fetus, 260 mm. in length, was also included. The data are given in the accompanying table.

From the table it is apparent that the estimates are in keeping with those for the placental and fetal circulations cited. The blood content of the fetal lung is higher than might be expected. The value is 3.11 per cent for the fetal pig, and 5.31 per cent for the human fetus. Compared with the estimates of Wiggers [10] and de Jager [25] for the adult lung, a rather profuse intra-uterine pulmonary circulation is shown, their values varying from 5.3 to 9 per cent. The intra-uterine circuit however, may be bronchial rather than pulmonary, although this is hardly the case. Coryllos [10] claimed that there is no blood in the pulmonary circuit before birth; Ziegenspeck [26] maintained that 50 per cent of the

25. de Jager, S.: Arch. f. d. ges. Physiol. **27**:152, 1882.
26. Ziegenspeck, R.: Samml. klin. Vortr., 1905, no. 401, ser. 14.

contents of the right ventricle is diverted to this channel, and Pohlman estimated that 20 per cent is probably more nearly correct. Be this as it may, the more significant point is that the antepartum pulmonary circulation is practically negligible as compared to the vast placental load, representing 3.11 per cent of the total load against 38.5 per cent.

An evaluation of the shift in load at birth may now be undertaken. The total load of the heart may be placed at 350 cc., distributed equally between the right and left ventricles. The load of each, then, is 175 cc. With the obliteration of the placental circulation, the total load is reduced to 250 cc. Based on the flow through the adult lung, as given by Wiggers,[27] from 10 to 20 per cent of the blood is in the pulmonary circuit, or from 25 to 50 cc. This represents the special load of the right side of the heart. Subtracting this amount from the total load, the load of the left side of the heart becomes 200 or 225 cc. Its previous load had been 175 cc., involving in part also the distant placental circulation. It is thus thoroughly capable normally of maintaining the systemic load without markedly increasing its rate. It is evident from this that the work of the right ventricle has been primarily to carry the load of the placental circulation.

At birth, the right side of the heart is required to move only 25 or 50 cc. of blood through the lesser circulation, although its previous capacity was 175 cc. It becomes apparent that a tremendous reserve force is present, which is suddenly thrown against the resistance of the capillary bed of the pulmonary circuit, a mechanical factor which in itself may act to assist in the dilatation of the alveoli.

We have tested this factor by inserting a cannula in the conus arteriosus, and after ligation of the ductus arteriosus, raising the pressure to 60 mm. of mercury, the normal systemic pressure at birth. The lungs in the stillborn infant were made to "inflate" strikingly after the fashion shown when a tracheal cannula is inserted and artificial respiration is induced in the cat. Histologic section of these lungs showed a marked distention of the walls and lumens of the alveoli.

On the basis of the foregoing considerations it is of interest to review the observed changes in the heart rate at birth. On the theory that the pulmonary circulation is established as the first step, the total load of the left side of the heart would become 350 cc., less 50 cc. diverted to the lung, or 300 cc. This would call for an acceleration, in proportion to its former load of 175 cc., of 230 beats per minute from the antenatal rate of 134. This should continue until pulsation ceases. With the obliteration of the umbilical circulation, the rate should again drop. This, however, is not the case, since an accelerated rate of from

27. Wiggers, C. J.: Physiol. Rev. **1**:239, 1921.

170 to 180 is maintained for from fifteen to thirty minutes, and even then deceleration is slow and gradual.

Since it is evident that the theory of diversion of flow to the lung cannot be the primary factor in accomplishing the shift, we may next consider the alternate hypothesis of spontaneous occlusion of the umbilical arteries and their effect on the systemic and pulmonary pressures and on the respiratory center.

The evidence for the spontaneous occlusion of the umbilical arteries is both histologic and experimental. Occlusion occurs normally in animals without ligation of the cord. Obstetric experience bears out the same fact for the human being. The musculature of the arteries at the umbilicus, the valves of Holokenius and the spiral course aid in ready occlusion. A warmed cord will frequently bleed spontaneously (Haselhorst [28]). Henneberg (cited by Haselhorst) has shown that new-born rats will die of asphyxia and umbilical hemorrhage if immersed to the neck in warm water.

We have attempted to perfuse a chilled human cord through a cannula in the fetal end of the umbilical artery, and have repeatedly failed with a pressure of 250 mm. of mercury. This is of interest since the normal pressure of flow in the umbilical artery before delivery at cesarean section is given at from 38 to 68 mm. by Haselhorst.[28] With the high pressure used, the chilled cord showed segmental circular constrictions at intervals of approximately 2 cm. The constrictions could be progressively relieved by long continuation of the high pressure. The flow was free, but slow, if the cannula was inserted 10 cm. from the placental insertion of the cord.

Thrombosis played no part in the occlusion. Neither was the substance of the cord immediately concerned, since the resistance at the constrictions was not relieved when the arteries were dissected free.

The nature of the stimulus to contraction of the umbilical arteries is still problematic. While it is generally considered to be cold, Ahlfeld has shown that contractions occur when the infant is delivered into a warm bath, the first respiratory movements being initiated with the child fully immersed. Schmitt [29] (1900) expressed the belief that the high oxygen concentration of the blood subsequent to breathing is the cause of occlusion. Haselhorst, however, pointed out that occlusion may occur before respiration, or pulsations may continue five minutes after respiration is well established. He further supported his view by measurements of the oxygen content of the umbilical arteries, which increases from 3 to 10 per cent by volume within the first two minutes. Whether

28. Haselhorst, G.: Ztschr. f. Geburtsh. u. Gynäk. **95**:400, 1929.

29. Schmitt, W., in Oppenheimer, C.: Handbuch der Biochemie des Menschen und der Tiere, Jena, Gustav Fischer, 1900, pp. 67 and 75.

the response is local or reflex is not definitely known, since nerves have been described only from the immediate vicinity of the umbilicus (Minot [30]). Haselhorst has shown a local reaction by severing the cord at 30 cm. from the umbilicus, which results in a temporary hemorrhage and subsequent occlusion with pulsation continued proximally. With each new section made nearer and nearer the umbilicus, hemorrhage and occlusion were repeated. We have personally verified these results.

Haselhorst has shown further that this occlusion is spontaneous, by resecting a piece of cord between two clamps. On the insertion of a needle attached to a mercury manometer, the pressure rose immediately to 24 mm. and continued to rise to 64 mm. within the next five minutes. He indicated, however, that complete obliteration does not always follow at once, since after the injection of methylene blue (methylthionine chloride, U. S. P.) into the umbilical arteries after delivery the dye may subsequently be detected in the urine of the infant. Hence, he premises a marked interference but not complete obliteration. In either event, partial or complete, the peripheral resistance in the vascular bed is tremendously increased, and we may next compare the effect with that produced by occlusion of the aorta in experimental animals, since the umbilical arteries present a carrying capacity only slightly short of that of the aorta.

Guthrie and Pike [31] have demonstrated that occlusion of the aorta, either abdominal or thoracic, is followed by a marked rise in systemic pressure. Furthermore, occlusion constitutes a marked respiratory stimulus which persists even with the vagi cut. Schmidt [1] has shown that cerebral flow is one of the three principal factors in the control of respiration. Hill and Macleod [32] have demonstrated that the cerebral flow is dependent directly on aortic pressure. Any factor that increases the peripheral resistance to the extent of raising the systemic pressure will increase the cerebral flow and constitute a respiratory stimulus, particularly in the apnea of "reversal."

We have presented evidence that the heart at birth possesses considerable reserve force due to the elimination of one third of its load; that the rate of contraction is increased rather than decreased, and that the umbilical circulation spontaneously occludes. The expected result should be a rise in systemic pressure. Cohnheim and Zunst [33] obtained a slight rise in pressure in the umbilical arteries of fetal goats immediately after delivery by cesarean section. Haselhorst [28] gave the predelivery pressure in one case as 68 mm. of mercury, and measured the

30. Minot, C. S.: Textbook of Embryology, Philadelphia, P. Blakiston's Son & Co., 1910.

31. Guthrie, C., and Pike, F. H.: Am. J. Physiol. **16**:475, 1906.

32. Hill, L., and Macleod, J. J. R.: J. Physiol. **26**:384, 1900.

33. Cohnheim, J., and Zunst, N.: Arch. f. Physiol. **17**:334, 1892.

postdelivery pressure in eight other cases. With three exceptions, the latter were the higher, being, respectively, 84, 74, 62, 70, 62, 92, 46 and 110 mm. In the three cases, there may already have been some local contraction in the umbilical arteries between the cannula and the umbilicus, as these pressures were recorded in the umbilical arteries.

Haselhorst's case 8 is of extreme interest, since the pressure was taken as respiration was initiated. The initial pressure was 60 mm., with a slight drop and rise between 70 and 60 before the first movements were noted. Just before or with the first cry the pressure rose to 100 mm. Considering the technical difficulties involved in securing these data, the observations are tremendously significant, and the experimental results bear out the theoretical expectations. The apnea of intra-uterine life is due to a "reversal" of the respiratory center produced by a physiologic anemia of developmental origin. Occlusion of the umbilical arteries increases the peripheral resistance in the aorta, raises the systemic pressure and induces a marked cerebral flow. This relieves the apnea; the high carbon dioxide concentration prevailing acts as a respiratory stimulus, and respiration is initiated.

That this view is not purely theoretical is shown further by the observations of Craigie [34] on the progressive vascularization of other centers in the brain stem during the first ten days of life in the rat. He was unable, however, to find evidence of gross vascular changes in the respiratory center at birth.[35] We have repeated his observations on the relative vascularity of the respiratory center in a 19 day old rat and in a new-born rat. The results were negative so far as measurable differences were concerned. On reflection, however, this would be expected, since temporary increases in pressure and cerebral flow would not be discovered by the histologic method.

The diffuse character of the respiratory center, coordinating as it does the facial, vagus, phrenic and intercostal nerves, also favors the postulate of a rather general mechanism for its control. The increased rate of the heart at birth is consistent with the hypothesis of a necessity for the maintenance of a high pressure. Furthermore, the initiation of respiration is not a purely reflex act, since the period of latency ranges normally from twenty to thirty seconds (Eastman [19]). Piestic factors alone give a coordination to all the variants in the normal process, and at the same time allow a rational explanation of the conditions existing in the pathologic states.

Thus, in the condition of atelectasis, the left side of the heart, exerting its pressure influence through the ductus arteriosus, may assist the right side in the removal of the peripheral resistance in the pulmonary

34. Craigie, E. H.: J. Comp. Neurol. **38**:27, 1924.
35. Craigie, F. H.: J. Comp. Neurol. **42**:57, 1926.

circuit. Again, when there are cerebral hemorrhage and asphyxia, the right side of the heart may assist the left side in maintaining the pressure necessary to vascularize the respiratory center. These concepts are in keeping with the observations on delayed closure of this important channel in these conditions. Collapse and obliteration occur only after a complete adjustment of the piestic factors concerned in maintaining flow through these two pathways.

We digress from the general problem at this point to consider a function of the ductus arteriosus which seems to have been overlooked. The equality of pressure in the aortic and systemic trunks, maintained by the ductus arteriosus, appears to be significant in providing an equalizing back pressure against which the semilunar valves, both aortic and pulmonary, develop, in order that they may be thoroughly competent to withstand their definite pressures. Were the pulmonaries dependent on the blood flow through the lung alone, it is readily apparent that they would be unable to withstand the load thrown on them at birth. We base this conclusion on an examination of the development of these valves normally and in the various anomalies such as pulmonary stenosis, coarctation, transposition of the great vessels and cor biloculare.

CLINICAL SIGNIFICANCE

The significance of any concept lies in its direct applicability to clinical conditions. Not only does the interplay of piestic factors at birth give a rational explanation to an otherwise obscure process, but light is thrown on the etiology of asphyxia neonatorum and cerebral hemorrhage in the new-born.

Two factors are generally invoked to account for cerebral hemorrhage, namely, tentorial tears due to forceps in difficult labors or an abnormal clotting mechanism. The first factor is apparently self-explanatory; the second obviously requires an additional factor to account for the extravasation. Pearce [36] has reviewed the relationship between cerebral hemorrhage and asphyxia neonatorum. In the pathology of asphyxia he has described massive hemorrhage and petechiae, not only in the brain stem with interference with the respiratory center, but in many other organs and membranes, such as the pleurae, pericardium and pia. The exact site is often obscure because of the general congestion. Yagi [37] mentioned subdural, leptomeningeal, intraventricular, intracerebral and epidural hemorrhages due to stasis, pressure and resistance. Kugelmass [38] stated that hemorrhage occurs in the sclera

36. Pearce, N. O., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 4, p. 382.

37. Yagi, H.: Jap. J. Obst. & Gynec. **12**:335, 1929.

38. Kugelmass, I. N.: M. Clin. North America **14**:1523, 1931.

and fundus of the eye in 20 per cent of new-born infants. Lundqvist [39] reviewed intrathoracic and intra-abdominal hemorrhage. Certainly, all of these widely distributed lesions cannot be accounted for on the theory of vascular tears, since they frequently occur in easy spontaneous delivery and in a few cases in cesarean section. Irving (1931), in reviewing one hundred and eighty-two autopsies in the new-born, stated that 40 per cent showed intracranial hemorrhage. Of these, 0.3 per cent occurred in cesarean section, 0.4 per cent in easy normal delivery and 2.6 per cent in breech presentation. In one series, one-half the infants dead from intracranial hemorrhage showed hemorrhage at other sites. The phenomenon of multiple hemorrhage is so common that Grier [40] based his diagnosis of asphyxia on petechial hemorrhage into the walls of the viscera.

Vascular injury, extravasation and asphyxia have been widely discussed. Wells,[41] in reviewing the subject, stated that it is difficult to imagine injury to the capillary walls due to a lack of nourishment or to an increased carbon dioxide content. Petechiae are not common in all cases of "air hunger" or in acid poisoning.

A "hemorrhagic diathesis" associated with a prolonged clotting time has been called on to explain cerebral hemorrhage and asphyxia (Rodda [42]). Sharpe and Maclaire,[43] in discussing a large series of cases of cerebral hemorrhage, showed an increase in spinal fluid pressure, and in many instances blood in the spinal fluid without a delayed clotting time. Some cases with delayed clotting time showed no hemorrhage.

One neglected factor in extravasation is capillary pressure. It is of interest to note that in the original series of cases of purpura discussed by Duke,[44] one patient showed petechiae while straining at stool, and a rise in capillary pressure is postulated to account for at least one factor in this condition. Furthermore, Pearce [36] listed as one of the characteristics of asphyxia marked distention of the right ventricle and larger vessels and extravasation of serous fluid into the peritoneal cavity.

While asphyxia and cerebral hemorrhage are generally considered to be causally related, it is not always clear which is cause and which

39. Lundqvist, B.: Acta obst. et gynec. Scandinav. **9**:331, 1930.

40. Grier, R. M.: Am. J. Obst. & Gynec. **22**:890, 1931.

41. Wells, H. G.: Chemical Pathology, Philadelphia, W. B. Saunders Company, 1914.

42. Rodda, F. C.: Studies with a New Method for Determining the Coagulation Time of the Blood in the New-Born, Am. J. Dis. Child. **19**:269 (April) 1920.

43. Sharpe, W., and Maclaire, A. S.: J. Obst. & Gynæc. Brit. Emp. **32**:79, 1925.

44. Duke, W. W.: The Pathogenesis of Purpura Hemorrhagica with Especial Reference to the Part Played by Blood-Platelets, Arch. Int. Med. **10**:445 (Nov.) 1912.

effect. Ford [45] was unable to produce lesions of the brain in kittens by asphyxia. Fragility of the vessels in premature infants seems to be a predisposing factor, since 150 mm. suction pressure causes hemorrhage in this condition. It is difficult to conceive of a mechanism involving hemorrhage into the intradural or intraventricular spaces that could materially affect the respiratory center except in terms of maladjustment of the cerebral pressure after vascular insult. Since vasomotor effects in the cerebral vessels may be ruled out, it would become impossible to maintain a sufficient cerebral flow to vascularize the respiratory center and relieve the intra-uterine apnea in cases of continued hemorrhage from a large tear or multiple petechial hemorrhage.

Certainly, in view of the high arterial pressures recorded by Haselhorst of 100 mm. of mercury, capillary pressure, stasis, rupture and extravasation can no longer be neglected as physiologic factors capable of producing both the hemorrhage and, secondarily, the asphyxia.

We have undertaken to test the effect of pressure within the range of normal at birth by injecting metallic mercury into the circulation of a stillborn infant, allowing a gravity flow until no more would pass. A plate was then taken. The injection was then renewed and maintained until a mercury manometer recorded a pressure of 60 mm. A second plate was then taken. The results were inconclusive primarily because pressures could not be accurately controlled. A second attempt was made, 10 per cent sodium iodide being used as the perfusing fluid, but the vessels were not sharply outlined, probably because of too much diffusion. We believe the method adaptable, however, and shall repeat it, using the oxychloride of bismuth method of Hill.

We believe that the concept of hyperpiestic adaptation at birth and its relief of apnea gives a rational explanation to the success attained by the Drinker respirator. Murphy, Wilson and Bowman [46] reported recovery from asphyxia in one case, one hour and fifteen minutes after delivery. This can mean only that oxygenation was carried on by the lungs during the prolonged interval in which some factor other than the carbon dioxide or oxygen concentration held the respiratory center in abeyance. During this period, the vascular regulatory mechanism concerned with the establishment of the normal threshold of stimulation of the center finally became effective and normal, controlled respiration resulted.

SUMMARY

1. Measurements were made of the blood volume of placental, systemic and pulmonary circulations in fetal pigs.

45. Ford, F. R.: Bull. Johns Hopkins Hosp. **42**:70, 1928.

46. Murphy, D. P.; Wilson, R. B., and Bowman, J. E.: Am. J. Obst. & Gynec. **21**:528, 1931.

2. Calculations are presented dealing with the shift in load of the right and of the left side of the heart at birth, and the significance to the mechanics of inflation of the lung and initiation of respiration is discussed.

3. A unilateral pneumothorax was produced in a kitten while it passed the birth canal, and a subsequent histologic comparison of the two lungs showed a profuse flow before respiration was initiated.

4. Perfusion pressures through a chilled human cord were examined and considered on the theory of spontaneous occlusion versus systemic collapse.

5. A theory of interplay of piestic factors at birth has been developed and discussed which gives a rational explanation of the initiation of respiration at birth.

6. The theory of shifting load and changing pressures is discussed in relation to the more obscure features of asphyxia neonatorum.

SCHILLING BLOOD COUNT IN THE PNEUMONIAS OF INFANCY AND OF CHILDHOOD

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In a previous study [1] the value of the Schilling blood count was determined in various infections of childhood. It was found that certain definite changes occurred in the blood smear with regularity, and that the course of an illness could often be anticipated by a daily differential count. An increase in the healthy and degenerated immature, polymorphonuclear neutrophil cells was noted at the height of infection. There were also lymphopenia and aneosinophilia. A decrease in the young forms with a return of the lymphocytes and the eosinophils indicated improvement somewhat in advance of the clinical signs.

The present work is devoted to repeated examinations by the Schilling method of the leukocytic changes in the blood of infants and children acutely ill with pneumonia.

LITERATURE

Kohlman [2] made Schilling blood smears in fifty cases of lobar, bronchial and influenzal pneumonia in adults. He concluded that this count gives prognostic aid, which coincided with the outcome in 76 per cent of the cases, and that this type of examination of the blood is of distinct value in the assessment of clinical findings, though it is not to be considered as a more important guide than the clinical findings.

In a similar study of general infections, which included pneumonias of adults, Weiss [3] reported that the percentage of immature cells is by far more valuable in prognosis than the total leukocyte count or the percentage of neutrophils.

In the pneumonias of infancy and childhood there has been but one brief study of five cases by Stettner.[4] His work, reviewed after the

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From the A. Jacobi Division for Children of the Lenox Hill Hospital, Service of Dr. Jerome S. Leopold.

1. Rogatz, J. L.: The Schilling Blood Count in the Prognosis of Acute Infections in Infancy and Childhood, Am. J. Dis. Child. **40**:70 (July) 1930.

2. Kohlman, S. H.: The Schilling Index as an Aid in the Prognosis and Diagnosis of Complications in Pneumonia, M. J. & Rec. **133**:182 (Feb. 18) 1931.

3. Weiss, A.: Newer Hematological Aspects of the Neutrophils in Infections, Am. J. M. Sc. **174**:45, 1927.

4. Stettner, E.: Leukocytenbild bei der genuinen Pneumonie des Kindes, Ztschr. f. Kinderh. **43**:122, 1927.

present study was in progress, showed results generally similar to those to be described in this paper. More recently Nussbaum [5] reported Schilling counts in a series of pediatric cases, which included a small group of cases of pneumonia.

PROCEDURE

In observing the reactions of the polymorphonuclear neutrophil cells during the pneumonias of infancy it was considered desirable to limit this study as far as possible to cases uncomplicated by superimposed infections, which would tend to confuse the blood picture due to the pneumonia itself. This was difficult, and the study was consequently prolonged. Of two hundred cases of pneumonia studied during this period less than 25 per cent were without complications. Of the cases which this work comprises, nine showed complications late in the illness or during convalescence; in five there was purulent otitis media, and in four, empyema. These infections were reflected in the blood picture, and it was not felt necessary to exclude them for this reason.

This report, then, is made from observations on fifty-one consecutive cases of juvenile, lobar and bronchial pneumonia, which ran a fairly typical course, uninterrupted by early complications. Most of the cases were confirmed by roentgen examination, and the differential smears were made daily, at the same hour in the morning. In several of the cases of lobar pneumonia blood smears were made twice daily as the probable day of crisis was approached, in order that the changes occurring at this period might be noted more accurately. Occasionally, significant changes in the cell counts could not be demonstrated in advance of the fall in temperature, but they were noted simultaneously therewith or shortly thereafter. This happened in very few instances, however, it having been possible to anticipate a clinical change by examination of the blood in 80 per cent of the cases. The changes were simultaneous with recovery in seven cases. If more frequent counts had been made in these children during the twenty-four hours preceding the fall in temperature, it is likely that this improvement would have been forecast in most of this group as well. In three cases improvement in the blood followed clinical improvement. This lag covered a period of from twenty-four to thirty-six hours (table 1).

An initial total leukocyte count was made in all cases and repeated daily in the earlier cases. These figures are omitted as being of minor importance in this study. All patients showed the usual hyperleukocytosis at the height of infection. Meyer [6] demonstrated that the mor-

5. Nussbaum, S.: The Schilling Hemogram; Its Application in Pediatrics, Arch. Pediat. **49**:207 (April) 1932.

6. Meyer, H. F.: Prognostic Significance of the Leucocyte Count in Penumonias of Children, Am. J. M. Sc. **181**:245 (Feb.) 1931.

tality is inversely proportional to the total count in the pneumonias of children. This, however, does not invariably follow. In case 17 there was a leukocyte count of 10,000, which, with the clinical signs, justified a poor prognosis, but the patient recovered.

TABLE 1.—*Analysis of Cases*

Case	Date	Age	Type	Compli-cation	Result	Result Shown in Blood	Per Cent Total Young Forms at Height of Infection
1	10/ 8/30	12 mos.	Bronchial	None	Recovered	24 hrs. ahead	48
2	10/11/30	5 yrs.	Lobar	None	Recovered	12 hrs. ahead	60
3	10/10/30	6 mos.	Bronchial	None	Recovered	24 hrs. ahead	48
4	10/19/30	4 yrs.	Lobar	None	Recovered	Simultaneous	67
5	12/ 6/30	3 mos.	Bronchial	None	Recovered	12 hrs. ahead	33½
6	12/19/30	3 yrs.	Lobar	None	Recovered	Simultaneous	53½
7	12/23/30	20 mos.	Lobar	None	Recovered	12 hrs. ahead	50
8	1/ 3/31	18 mos.	Lobar	O.M.P.A.*	Recovered	24 hrs. ahead	47½
9	1/ 4/31	18 mos.	Lobar	O.M.P.A.	Recovered	48 hrs. ahead	54½
10	1/ 5/31	5 mos.	Bronchial	None	Recovered	24 hrs. ahead	29½
11	1/ 7/31	2 yrs.	Lobar	O.M.P.A.	Recovered	24 hrs. ahead	40
12	1/10/31	2½ yrs.	Bronchial	O.M.P.A.	Recovered	24 hrs. ahead	50
13	1/25/31	6 yrs.	Lobar	None	Decovered	12 yrs. ahead	63
14	2/13/31	4 yrs.	Lobar	None	Recovered	24 hrs. after	39
15	2/18/31	3½ yrs.	Lobar	None	Recovered	48 hrs. ahead	54½
16	3/ 4/31	4 yrs.	Lobar	None	Recovered	24 hrs. ahead	49
17	3/ 8/31	4 yrs.	Lobar	None	Recovered	24 hrs. ahead	66
18	4/ 1/31	2 yrs.	Bronchial	None	Expired	24 hrs. ahead	55½
19	4/29/31	17 mos.	Lobar	O.M.P.A.	Recovered	36 hrs. ahead	50
20	5/20/31	2 yrs.	Hilar	None	Recovered	24 hrs. ahead	39½
21	10/21/31	19 mos.	Lobar	None	Recovered	Simultaneous	31½
22	11/ 2/31	6 mos.	Lobar	None	Recovered	12 hrs. ahead	27
23	11/10/31	17 mos.	Bronchial	None	Recovered	24 hrs. ahead	61
24	11/13/31	7 yrs.	Lobar	None	Recovered	12 hrs. after	53
25	11/14/31	21 mos.	Lobar	None	Recovered	12 hrs. ahead	43
26	12/13/31	7 yrs.	Lobar	None	Recovered	Simultaneous	53
27	12/13/31	7 yrs.	Lobar	None	Recovered	Simultaneous	43
28	12/15/31	2 yrs.	Bronchial	O.M.P.A.	Recovered	24 hrs. ahead	59
29	12/26/31	3 yrs.	Bronchial	None	Expired	24 hrs. ahead	70
30	12/27/31	2 yrs.	Lobar	None	Recovered	24 hrs. ahead	48
31	1/ 3/32	9 yrs.	Lobar	None	Recovered	24 hrs. ahead	61
32	1/ 8/32	3 yrs.	Lobar	None	Recovered	24 hrs. ahead	53½
33	1/21/32	5 yrs.	Lobar	Empyema	Recovered	24 hrs. ahead	52
34	2/11/32	9 yrs.	Lobar	Empyema	Recovered	Simultaneous	54
35	2/22/32	6 mos.	Bronchial	None	Recovered	24 hrs. after	45½
36	2/22/32	2 yrs.	Lobar	None	Recovered	24 hrs. ahead	69
37	2/23/32	8 mos.	Lobar	O.M.P.A.	Recovered	60 hrs. ahead	50½
38	2/26/32	18 mos.	Bronchial	None	Recovered	60 hrs. ahead	48
39	3/ 3/32	3 wks.	Bronchial	None	Recovered	24 hrs. ahead	67
40	3/ 5/32	17 mos.	Lobar	O.M.P.A.	Recovered	12 hrs. ahead	50½
41	3/25/32	16 mos.	Bronchial	T.B.	Expired	48 hrs. ahead	58
42	4/ 5/32	6 yrs.	Lobar	None	Recovered	24 hrs. ahead	59½
43	4/ 7/32	4 yrs.	Hilar	None	Recovered	24 hrs. ahead	53½
44	4/11/32	3 yrs.	Bronchial	T.B.	Expired	72 hrs. ahead	67
45	4/12/32	8 yrs.	Lobar	Empyema	Improving	36 hrs. ahead	59
46	4/18/32	6 yrs.	Lobar	None	Recovered	Simultaneous	65½
47	4/27/32	2 yrs.	Bronchial	None	Recovered	24 hrs. ahead	61½
48	4/24/32	2 yrs.	Bronchial	None	Recovered	24 hrs. ahead	72
49	4/29/32	2½ yrs.	Bronchial	None	Expired	24 hrs. ahead	.2½
50	5/14/32	2 yrs.	Bronchial	None	Recovered	36 hrs. ahead	31
51	5/21/32	2½ yrs.	Lobar	None	Recovered	48 hrs. ahead	44

* O.M.P.A. indicates acute purulent otitis media.

The total number of counts made was five hundred and two, representing an average of about ten counts per patient. Two hundred cells were counted in each smear.

Charts of selected cases have been prepared, showing the temperature curves and values for the lymphocytes, monocytes, eosinophils and juvenile forms. The curve representing the total percentage of neutrophils has been omitted in this work, since it approximately follows the direction of the immature neutrophils, but deviates at important points and is therefore not nearly so accurate for judging the prognosis. During recovery, as the immature cell curve falls to normal, the line of the total polymorphonuclears rises to assume its normal level in the chart and can hence be no guide in determining the outcome, as some have thought. Whereas an increase in the immature cells would indicate new infection somewhere in the body, an increase in the total neutrophils may not have this same significance (chart 3).

OBSERVATIONS

Patients were generally admitted to the service during the second or third day of the pneumonia. At this time a differential smear of the blood showed marked neutrophilia with an unusually high percentage of staff cells or degenerated immature neutrophils, the nuclei of which had failed to segment (variously termed *Stabkernige* or *Stab* or *Band* forms). They constituted from 50 to 60 per cent of the leukocytes at the height of infection—a somewhat greater number than one finds in adults under similar conditions, indicating, perhaps, a more active response of the bone marrow to irritation from bacterial toxins.

The staff cells showed marked evidence of degeneration, being small and poorly developed, with deep-staining, pyknotic nuclei, excessive irregular, coarse granulations in the cytoplasm (toxic granulations of Mommsen [7]) and frequent vacuolization. These forms stained so intensely at the height of the illness that it was at times difficult to distinguish clearly the characteristics of the cell in some areas of the smear.

In addition to this predominance of staff cells, there was lymphopenia. There were fewer mature, segmented cells than are normally present and no eosinophils. The blood platelets, which are ordinarily scattered throughout the smear and visible in almost every field, were seen occasionally. This observation has not been checked by quantitative counts in this study.

As the infection proceeded, the shift to the left was further increased by additional staff forms and the appearance of healthy, juvenile cells not yet acted on by peripheral toxins in the blood stream. Unable to

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7. Mommsen, H.: Ueber die neutrophilen Granulationen der Leukocyten und ihre gesetzmässige Veränderung bei Scharlach und lobarer Pneumonie, Jahrb. f. Kinderh. **116**:293, 1927. Kugel, M. A., and Rosenthal, N.: Pathologic Changes Occurring in Polymorphonuclear Leukocytes During the Progress of Infections, Am. J. M. Sc. **183**:657 (May) 1932.

produce mature, segmented neutrophils rapidly enough to meet the increased demand, the bone marrow throws these immature forms into the blood. If this irritation continues, myelocytes appear. An increasing and persistent shift to the left from this point indicated a poor prognosis (case 18).

Preceding the fall in temperature or the appearance of other signs of clinical improvement by from twelve to twenty-four hours or more, the juvenile and the staff cells decreased rapidly and often suddenly. A corresponding increase in the number of segmented cells and lymphocytes occurred. With resolution one noted a much healthier appearance of the mature forms. These cells were larger, and the nucleoplasm took the stain less intensely. The cytoplasm stained more evenly, containing fewer and finer granulations, and showed only occasional or no vacuolization. There was a reappearance of blood platelets in great clumps throughout the smear. This finding was so constant that it was frequently possible to judge improvement from this fact alone. The reappearance of eosinophils was also a favorable sign confirming recovery.

TABLE 2.—*Form of Hemogram*

B	E	M	J	St	S	L	Mon
			Shift				
			Neutrophils				

A variable monocytosis accompanied convalescence. The blood reached normal between two and twelve days after the fall in temperature, usually after about ten days.

REPORT OF CASES

In the following review of cases only several have been chosen of those which most strikingly illustrate the changes described. The hemogram and the chart are used. The hemogram is a convenient, horizontal tabulation of the leukocytes counted and is presented in several of the cases with the following abbreviations: B, basophil; E, eosinophil; M, myelocyte; J, juvenile; St, staff; S, segment; L, lymphocyte; Mon, monocyte.

The summation of myelocytes, juveniles, staffs and segments comprises the total neutrophil count of which the myelocytes, juveniles and staffs form the immature cell count or significant "shift to the left" when increased over normal. It is this figure which indicates the presence of infection and which is most important in this study.

CASE 13.—J. M., 5 years old, was admitted to the hospital on January 25 with a temperature of 103 F. due to acute pneumonia of the lower lobe of the left lung. There was a marked shift to the left in the blood consisting of almost 60 per cent immature forms. Myelocytes appeared during the next few days. A fall in

temperature to 98.6 F. on January 27 was preceded by a decrease in the immature cells but accompanied by a further shift to the left, indicating that this was not a true crisis. The temperature rose again to 104 F. On January 28, however, there was a marked decrease in the shift with a reappearance of eosinophils and a rise in the number of lymphocytes. These favorable signs were followed by a true crisis twelve hours later. The blood cells rapidly approached their normal relations during the next five days (chart 1).

Case 15.—M. S., aged 3½ years, ill three days with a temperature of 103 F., was admitted to the hospital with pneumonia of the lower lobe of the right lung. The usual blood picture was found with over 40 per cent staff cells, lymphopenia and aneosinophilia. During the succeeding two days the shift to the left increased. On February 21 the blood showed a decrease in shift and a corresponding increase

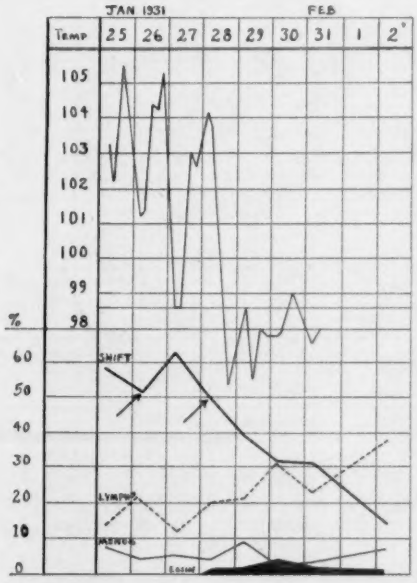

Chart 1 (case 12).—Note the fall in shift (immature forms) on January 26 (first arrow), followed the next day by a pseudocrisis, indicated by a simultaneous rise in shift. A further fall in shift on January 28 (second arrow) was followed that night by a true crisis.

Table 3.—*Hemogram for Case 13*

Date	B	E	M	J	St	S	L	Mon
1/25/31	...	...	...	3.5	56.0	19.0	13.0	8.5
1/26/31	...	...	0.5	2.5	49.0	21.5	20.5	6.0
1/27/31	...	...	0.5	3.5	59.0	16.0	13.5	7.5
1/28/31	...	0.5	0.5	8.0	41.5	25.0	19.0	5.5
1/29/31	0.5	2.0	...	...	39.5	27.5	21.0	9.5
1/30/31	0.5	3.5	...	1.5	29.0	31.5	31.5	2.5
1/31/31	...	2.0	...	1.0	30.0	39.0	24.5	3.5
2/ 2/31	...	0.5	...	0.5	14.0	41.0	37.0	7.0

in lymphocytes, which were followed the next day by a further fall in shift and on February 23 by an abrupt fall in temperature, forty-eight hours after the first sign of improvement in the smear. From this point there was a slow return of the cells to normal (chart 2).

CASE 17.—G. F., aged 4 years, was admitted to the hospital with a temperature of 106 F. due to pneumonia of the upper lobe of the right lung of eight days' duration. The blood smear showed a marked left shift, which increased to more than 60 per cent of immature forms on the tenth day of the illness. Myelocytes were present. The total white cell count at this time was 10,000, which, with other signs,

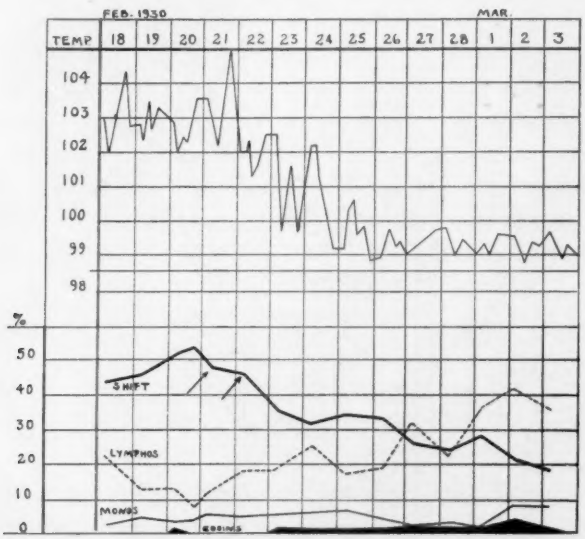

Chart 2 (case 15).—The two arrows indicate the fall in shift on two successive days, followed on the third day by a marked fall in temperature. Note the gradual return of the various elements to normal in about eight days.

TABLE 4.—*Hemogram for Case 15*

Date	B	E	M	J	St	S	L	Mon
2/18/31	...	...	...	1.5	43.0	29.5	22.5	3.5
2/19/31	0.5	...	...	0.5	45.0	35.5	13.0	5.5
2/20/31 a.m.	...	1.0	...	1.5	49.0	30.5	13.5	4.5
2/20/31 p.m.	...	...	...	3.0	51.5	31.5	8.5	5.5
2/21/31 a.m.	...	...	0.5	2.5	44.0	34.0	11.5	7.5
2/22/31	...	...	1.0	1.0	43.5	31.0	18.0	5.5
2/23/31	...	1.0	0.5	2.5	30.0	41.0	19.0	6.5
2/24/31	...	0.5	...	1.5	30.5	35.0	26.0	6.5
2/25/31	...	0.5	...	...	35.5	40.0	15.5	8.5
2/26/31	...	0.5	...	1.0	33.5	41.5	18.5	5.0
2/27/31	...	2.0	...	0.5	25.0	38.5	32.0	2.0
2/28/31	0.5	4.0	...	1.0	23.0	43.0	23.0	5.5
3/ 1/31	0.5	1.0	...	1.0	28.0	31.5	37.0	8.5
3/ 2/31	0.5	3.5	...	...	22.0	24.0	41.5	8.5
3/ 3/31	0.5	1.0	...	...	17.5	39.5	34.5	7.0

suggested a poor prognosis. The patient remained desperately ill despite the use of oxygen, and acute catarrhal jaundice developed. On the eleventh day of the illness, however, the staff cells decreased suddenly. This suggested a more favorable prognosis despite a persistently high temperature. On the following day the temperature fell rapidly, and the child recovered. It should be noted that the total neutrophil curve, which is shown in the chart for this case, gave no indication of the approaching improvement, but remained at a constantly high level until the second day after the fall in temperature (chart 3).

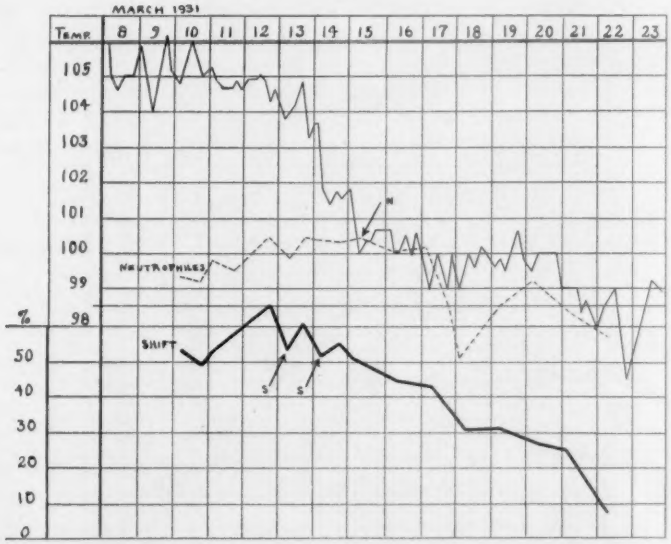

Chart 3 (case 17).—Arrows *s* indicate a fall in shift on two successive days followed by a crisis twenty-four hours later. Note that the neutrophil count does not indicate the approaching crisis in this case, but remains high (arrow *n*) for two days after the crisis.

TABLE 5.—*Hemogram for Case 17*

Date	B	E	M	J	St	S	L	Mon
3/10/31	...	...	...	13.0	36.5	21.5	22.5	6.5
3/11/31 a.m.	...	...	...	19.5	35.0	35.0	17.0	3.5
3/11/31 p.m.	...	...	...	7.0	51.0	17.0	21.0	4.0
3/12/31 a.m.	...	...	0.5	5.0	55.0	18.5	16.5	4.5
3/12/31 p.m.	...	...	1.0	7.0	58.0	18.5	13.0	2.5
3/13/31 a.m.	...	0.5	0.5	7.0	46.5	24.5	18.5	2.5
3/13/31 p.m.	...	...	...	3.5	57.5	25.0	9.5	4.5
3/14/31 a.m.	...	...	...	12.0	39.0	34.0	10.5	4.5
3/14/31 p.m.	...	...	...	9.0	47.5	27.0	16.0	5.0
3/15/31 a.m.	...	...	1.0	7.0	43.5	35.5	10.5	2.5
3/16/31 a.m.	0.5	...	2.5	1.5	41.0	35.0	15.0	4.5
3/17/31	0.5	...	1.0	2.0	40.0	38.0	16.5	2.0
3/18/31	...	1.0	...	3.0	28.0	23.0	22.0	6.0
3/19/31	0.5	0.5	...	1.0	31.5	34.0	25.0	7.5
3/20/31	...	...	...	2.0	24.0	45.0	25.5	3.5
3/21/31	0.5	1.5	...	3.5	21.5	38.0	30.5	4.5
3/22/31	...	...	...	0.5	9.0	49.0	36.5	5.0

CASE 18.—D. L., 2 years old, was admitted to the hospital on the seventh day of his illness with acute bronchopneumonia and a temperature of 105 F. The total number of immature cells was fewer in this instance than in the average case. However, it is more important to note the daily variations in cells than to know the actual percentages at any given moment. In this patient, for example, the

TABLE 6.—*Hemogram for Case 18*

Date	B	E	M	J	St	S	L	Mon
4/1/31	...	...	...	6.0	23.5	9.0	56.0	5.0
4/2/31	...	...	...	5.5	17.5	12.5	58.0	6.5
4/3/31	...	...	0.5	3.0	31.0	17.5	40.5	7.5
4/4/31	...	0.5	0.5	15.5	27.5	16.0	27.5	12.5
4/5/31	...	...	0.5	27.0	28.0	16.0	20.5	8.0

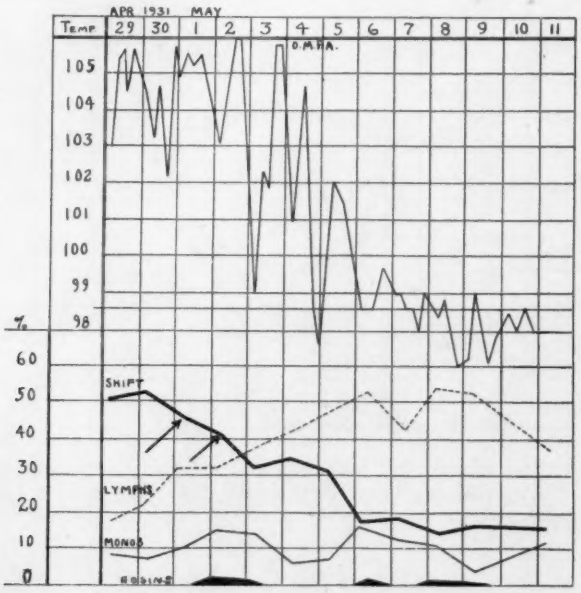

Chart 4 (case 19).—Arrows indicate a definite fall in shift on two successive days followed almost forty-eight hours after the first sign of improvement in the blood by a crisis on May 3. The secondary rise in temperature was due to otitis media.

TABLE 7.—*Hemogram for Case 19*

Date	B	E	M	J	St	S	L	Mon
4/29/31	...	...	...	1.0	49.0	23.0	18.0	9.0
4/30/31	...	...	...	1.5	50.5	20.5	20.5	7.0
5/ 1/31	0.5	...	...	5.5	39.0	14.5	30.5	10.0
5/ 2/31	...	1.5	...	3.0	39.0	10.0	31.0	15.5
5/ 3/31	0.5	1.0	...	6.0	26.5	16.0	35.5	14.5
5/ 4/31	...	...	...	3.0	33.0	14.0	43.5	6.5
5/ 5/31	...	...	...	1.0	31.5	14.0	46.5	7.0
5/ 6/31	0.5	0.5	...	...	17.5	11.5	53.0	17.0
5/ 7/31	...	...	...	...	18.5	25.5	43.0	13.0
5/ 8/31	...	1.0	...	...	15.0	20.0	53.0	11.0

steadily increasing shift to the left with the appearance of myelocytes and their persistence suggested a fatal prognosis, which the appearance of an isolated eosinophil on April 4 could not improve. On the next day the juvenile cells had increased to 27 per cent. Death occurred that night.

CASE 19.—M. R., aged 17 months, was ill for three days with a temperature of 104 F. and pneumonia of the lower lobe of the left lung. The blood showed the usual marked left shift, consisting mostly of staff forms. Despite the appearance of jaundice on the fifth day and a persistently high fever, a steadily decreasing shift and the appearance of eosinophils justified a favorable prognosis. A crisis did occur during the seventh night. The secondary rise in temperature was due to a bilateral, purulent otitis media, slightly reflected in the blood by a rise in staff cells, a decrease in lymphocytes and a disappearance of eosinophils. After paracentesis and drainage of the middle ears, the temperature and blood rapidly approached normal (chart 4).

CASE 29.—A. M., aged 3 years, was admitted to the hospital with diffuse, confluent bronchopneumonia involving both lungs. The temperature was 105 F. The duration was five days. The temperature remained between 105 and 106 F. The

TABLE 8.—*Hemogram for Case 29*

Date	B	E	M	J	St	S	L	Mon
12/26/31	...	...	1.5	13.0	35.5	19.0	29.5	1.5
12/27/31	...	...	1.0	14.5	36.5	27.0	19.0	2.0
12/28/31	...	...	2.5	20.5	35.5	16.5	21.5	3.5
12/29/31	...	...	2.0	20.5	47.5	7.5	20.0	2.5
12/30/31	Died							

child was only slightly cyanotic, but became markedly so on slight exertion. The edge of the liver was palpable about 1 inch (2.5 cm.) below the inferior costal margin and after two days was felt at the level of the umbilicus. The blood smear on admission showed a high juvenile and staff cell count with myelocytes present. These persisted throughout the remainder of the illness, while the immature forms increased daily, indicating a poor outcome. The leukocyte count was 10,000. The child died five days after admission.

CASE 23.—R. T., 17 months old, was admitted to the hospital with bronchopneumonia resulting in a fluctuating temperature, normal at night and 104 F. in the morning for the previous two weeks. Apart from signs at the base of the left lung, examination gave negative results. The infant was admitted at the end of this attack of pneumonia as indicated by the falling temperature and the decrease in immature cells of the blood. On the fourth day after admission, despite a normal temperature, the smear showed a sudden, marked shift to the left. The staff forms increased from 30 to 61 per cent. A rise in temperature was predicted and occurred the same afternoon, owing to a new area of bronchopneumonia. Continued decrease in the staff cells two days later, despite a temperature of 101 F., indicated recovery (chart 5).

CASE 41.—A. R., aged 16 months, was admitted to the hospital with a temperature of 105 F. and a history of cough and fever for the previous ten days. Examination revealed acute bronchopneumonia involving the upper lobe of the left lung

and the base of the right lung. A secondary anemia was present. The examination otherwise gave negative results. The temperature remained high until the fourth day after the patient's admission, when, coincidentally with a transfusion of blood, given because of the marked anemia, the fever began to subside by lysis, the temperature reaching normal two days later. Despite the transfusion and fall in temperature, blood smears showed an increasing shift to the left. In face of the evident clinical improvement the increase in staff forms and the appearance of juvenile cells were difficult to explain. On the sixth day, however, the temperature suddenly rose to 102.8 F., and a complete, left-sided hemiplegia involving the face and extremities was noted. Myelocytes appeared in the peripheral blood, and the

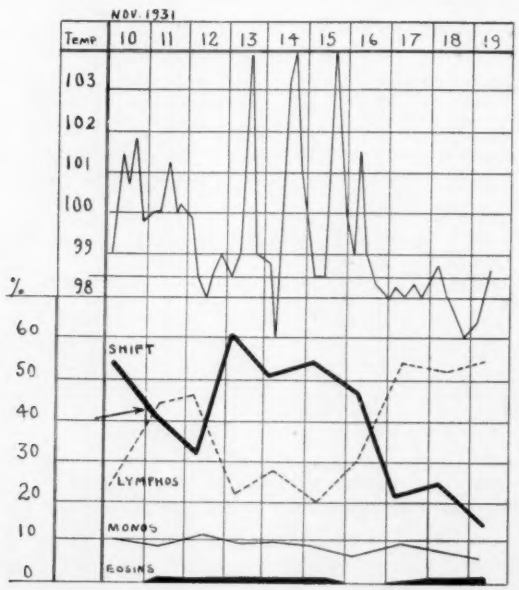

Chart 5 (case 23).—Note the fall in shift on November 11 (arrow), followed by a fall in temperature the next day. Note the sudden, severe shift to the left on November 13 with normal temperature, followed that afternoon by a rise to 104 F. and a rapid return of the blood to normal after the final fall in temperature.

TABLE 9.—*Hemogram for Case 23*

Date	B	E	M	J	St	S	L	Mon
11/10/31	...	...	...	1.5	53.0	10.5	25.0	10.0
11/11/31	...	0.5	...	2.5	40.0	7.0	44.0	6.0
11/12/31	1.5	1.5	...	1.5	30.0	9.0	46.0	10.5
11/13/31	...	0.5	...	...	61.0	8.5	22.5	7.5
11/14/31	...	0.5	...	3.0	48.0	13.0	27.5	8.0
11/15/31	...	0.5	...	0.5	55.0	17.0	20.0	7.0
11/16/31	...	...	...	3.5	43.0	18.0	30.5	5.0
11/17/31	...	2.5	...	1.0	21.0	11.0	57.0	7.5
11/18/31	0.5	1.5	...	...	25.5	10.0	56.5	6.0
11/19/31	...	2.0	...	...	17.0	9.0	57.0	5.0

patient died on the ninth day in the hospital. Autopsy showed generalized miliary tuberculosis with thrombosis of the cerebral vessels and an extensive hemorrhage covering the entire right side of the cortex of the brain. In this case the Schilling count clearly indicated an underlying infection of increasing severity in the face of a misleading temperature curve and clinical improvement (chart 6).

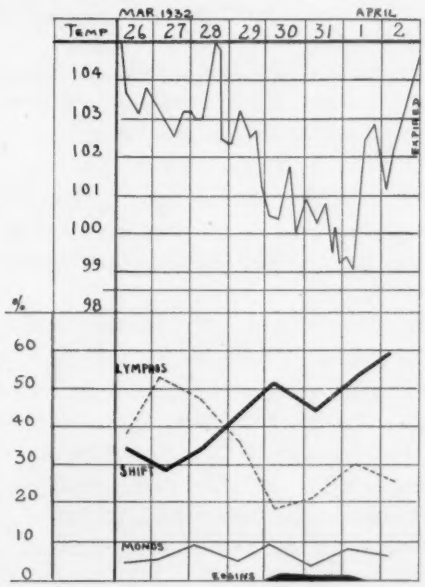

Chart 6 (case 41).—Note the daily increase in shift, despite the gradual fall in temperature to normal and the appearance of eosinophils, and the final justification of this shift curve by a sudden rise in temperature on April 1 and death on the night of April 2.

TABLE 10.—*Hemogram for Case 41*

Date	B	E	M	J	St	S	L	Mon
3/26/32	...	...	...	0.5	33.5	25.5	38.0	3.0
3/27/32	...	...	...	0.5	28.5	14.5	52.0	4.5
3/28/32	...	...	...	1.5	32.5	10.0	48.0	8.0
3/29/32	...	...	...	1.0	41.0	18.0	36.0	4.0
3/30/32	...	1.0	...	2.5	48.0	22.0	18.5	8.0
3/31/32	1.0	0.5	...	...	44.0	23.5	27.5	3.5
4/ 1/32	0.5	0.5	...	1.5	51.0	19.0	20.5	7.0
4/ 2/32	...	...	1.0	4.0	53.0	6.0	30.0	6.0
4/ 3/32	Died							

COMMENT

Summarizing the observations made on the blood in a series of cases of pneumonia in early childhood, repeated daily examination of the smears shows the following: At the beginning of infection there is a great increase in the percentage of degenerated, immature (staff) leukocytes at the expense of the mature, segmented forms and the lympho-

cytes. One finds lymphopenia and aneosinophilia. As the infection reaches its height there is a further increase in the staff forms, and healthy, juvenile cells appear, more than half the cells present usually forming this significant "shift to the left." Weiss stated that in early pneumonias in adults a count with 50 per cent immature forms generally means a fatal prognosis. This apparently does not apply in early childhood, for most of the cases studied showed between 50 and 60 per cent immature forms, and the patients recovered. Myelocytes may appear in the peripheral blood stream. Their persistence with continued increase in juvenile forms is indicative of a poor prognosis.

Evidences of marked degeneration are also found in the granulocytes, such as coarse, irregular granulations in the cytoplasm with deep-staining, pyknotic nuclei. The blood platelets seem greatly diminished, and are often almost absent from the smear. Their return is a sign of improvement.

As the infection subsides, a definite decrease in the immature forms and a corresponding increase in the mature cells and lymphocytes occur. There is usually monocytosis as well at this stage. The reappearance of eosinophils may be a further indication of recovery. These favorable signs precede the crisis by many hours in most cases of lobar pneumonia. During convalescence there are a further increase in lymphocytes, a rapid or gradual decline in the immature cells and a final return of the various cellular forms to their normal qualitative and quantitative relationships.

There has recently been a tendency, in reporting Schilling counts, to group the myelocytic, juvenile and staff forms simply as "immature cells" or "young forms." Satisfactory results may be obtained by this abbreviated method, but often the more accurate separation of young forms into the three simple groups described permits a more interesting and certainly a clearer image of the progress of an infection.

It seems clear from the foregoing observations that a study of the immature polymorphonuclear leukocytes in the blood gives one a more sensitive picture of what is happening in the body during its struggle to overcome infection than can be obtained from the ordinary blood smear, wherein mature and immature forms are simply grouped as polymorphonuclears. Though one would not care to rely exclusively on information received from the blood, the patient's condition and the progress of the disease are in most cases reflected with sufficient accuracy to make reliable suggestions as to prognosis possible.

CONCLUSIONS

Fifty cases of juvenile, bronchial and lobar pneumonia were studied with reference to changes occurring in the leukocytes during these infections. The Schilling classification of immature cells was used. The

daily changes in these elements of the blood were observed and are described in detail. It was possible to anticipate lysis in bronchial pneumonia or the occurrence of the crisis in the lobar types by many hours. Descriptions, with charts and hemograms, are given of striking cases, which illustrate this observation.

From these and other studies it is concluded that the Schilling blood count is of greater value than the ordinary smear in revealing changes in the patient's condition, that it reflects these changes more accurately and somewhat in advance of their clinical appearance and that it should therefore replace the usual differential examination of the blood in routine practice.

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LOSS OF MINERALS THROUGH THE SKIN OF INFANTS

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Quantitative determinations of minerals excreted by the skin of infants have received little consideration in the literature. Only one paper by Rominger and Meyer,[1] which bears directly on this subject, has come to our attention. A number of papers [2] deal with the mineral content of the sweat in the normal adult, in the sick adult and in the adult in whom sweating was induced artificially.

Rominger and Meyer [1] determined the combined amount of sodium and potassium as chlorides excreted through the skin of an infant fed on cow's milk. They concluded that the amount of sodium and potassium lost through the skin did not materially affect the differences in retention of these elements obtained in the breast-fed infants and in those fed cow's milk. In our extended study of this problem, it was our object to determine separately the amount of sodium, potassium, chlorine, calcium and phosphorus lost through the skin by infants fed cow's milk.

PROCEDURE AND METHODS

Five normal infants ranging in age from 2 to 24 weeks were used in the experiment. The room temperature was kept almost constant, ranging from 75 to 78 F., as registered by a thermometer on the inner wall. Before the experiment was begun, the skin of the infant was carefully cleansed. This cleansing consisted of a bath with soap and water, a careful sponging with tap water and a thorough rinsing with distilled water. The infant was then dried with linen which had been boiled and rinsed in distilled water to remove all the minerals. Next the infant was placed on a metabolism frame in order that the urine and stool could be collected separately. While on the frame, the infant was dressed in light clothing from which mineral salts had been removed. Two thicknesses of linen were placed

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From the Department of Pediatrics, the University of Chicago.

1. Rominger E., and Meyer, H.: Ueber die Mineralausscheidung durch die Haut beim Säugling, Ztschr. f. Kinderh. **47**:721, 1929.

2. Barney, R. E.: The Chemical Analysis of Sweat, J. A. M. A. **85**:1373 (Oct. 31) 1925; The Chemical Analysis of Sweat; Further Study, ibid. **87**:1827 (Nov. 27) 1926. Schwenkenbecker and Spitta: Ueber die Ausscheidung von Kochsalz und Stickstoff durch die Haut, Arch. f. exper. Path. u. Pharmacol. **56**:284, 1907. Pemberton, R.; Cajori, F. A., and Crouter, C. Y.: A Note on the Composition of Human Sweat, Ann. Int. Med. **2**:1243, 1929.

under the head to catch the sweat. A ruff of gauze was fastened loosely under the chin to catch the saliva from the drooling infant and any material that might be regurgitated. Every twenty-four hours the infant was given a bath in distilled water and a change of mineral-free clothing. The sweat was then extracted from the soiled clothing which was boiled in distilled water and carefully rinsed in the same kind of water. The bath water and the water from the extractions and rinsings were then combined and evaporated to a small volume. This procedure was followed for six days, and the concentrates for each twenty-four hours were pooled, filtered to free the solution from lint and made up to a suitable volume.

Quantitative analyses on the combined specimens of sweat were carried out as follows: (*a*) An aliquot was taken for the determination of chlorides by the method of Laudet.[3] (*b*) the remaining part of the solution was evaporated to dryness, ashed at 400 C., the ash dissolved in dilute nitric acid and made up to a known volume. On aliquots of this solution sodium was determined by the method

TABLE 1.—*The Loss of Minerals Through the Skin in Millimols per Day*

Infant	Age, Weeks	Weight, Gm.	Length of Period, Days	Potassium	Sodium	Chloride	Calcium	Phosphorus	Comment
O. I	2	3,485	6	0.24	0.17	0.22	0.07	0.01	Born at term
S. I	3	2,645	6	0.21	0.18	0.26	0.19	0.03	Premature
S. II	4	2,825	6	0.33	0.15	0.29	0.14	0.01	Premature
S. III	5	2,980	6	0.52	0.22	0.33	0.12	0.01	Premature
O. II	8	4,885	6	0.66	0.44	0.52	0.15	0.03	Born at term
O. III	11	5,715	6	0.71	0.34	0.61	0.15	0.03	Slight fever
D. I	14	5,655	6	1.74	0.66	0.88	0.23	0.01	Born at term
D. II	16	6,095	6	1.83	0.70	0.99	0.19	0.01	Born at term
M. I	16	5,120	6	1.86	0.94	1.48	0.15	0.26	Born at term
M. II	19	5,550	6	1.70	0.95	1.15	0.14	0.14	Born at term
M. III	21	5,830	6	1.39	0.65	0.90	0.14	0.04	Born at term
D. III	22½	6,880	6	1.65	0.66	0.82	0.16	0.02	Born at term
Mo. II	25½	7,105	6	1.54	0.50	0.78	0.16	0.01	Born at term
Mo. III	28	7,320	6	1.59	0.63	0.90	0.18	0.01	Born at term

of Butler and Tuthill,[4] potassium by the method of Fiske,[5] calcium by the method of Fiske and Logan[6] and phosphorus by the method of Fiske and Subbarow.[7]

Table 1 contains the data obtained on the sweat collected from five infants. Each period of investigation lasted six days, and four of the five infants were on the metabolism frame for eighteen days.

The results obtained show that during the first weeks of infancy the loss of minerals through the skin is small. The greater loss at 6 months, as shown by table 1, cannot be explained on the basis of surface area, since doubling of the weight only increases the surface area by one-third over the area at birth.

A second interesting finding, which contradicts the impression to be gained from the article of Rominger and Meyer,[1] concerns the potassium. Instead of representing a small fraction of the mineral loss through the skin, potassium is the largest fraction, then comes chlorine and finally sodium. The loss of the other two minerals, calcium and phosphorus, can scarcely be considered of any importance.

3. Laudet, M. M.: J. de pharm. et chim. **16**:168, 1917.
4. Butler, A. M., and Tuthill, E.: J. Biol. Chem. **93**:171, 1931.
5. Fiske, C. H., and Litarczek, G.: J. Biol. Chem. **67**:xvi, 1926.
6. Fiske, C. H., and Logan, M.: J. Biol. Chem. **93**:211, 1931.
7. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.

Table 2 shows our data compared with the results published by Rominger and Meyer.[1] The combined sodium and potassium lost through the skin is expressed as the sum of the chlorides. It may be seen that agreement is excellent for similar age periods.

Table 3 contrasts the retention of sodium, potassium and chlorine in breast-fed infants and in those fed on cow's milk after correction has been made for the loss through the skin. In the artificially fed infant of 3 months, the loss of potassium and chlorine through the skin lowers the retention figures for these minerals to values approximating the uncorrected retentions obtained in the case of the breast-fed infant. This equalization is not so striking in the 6 months' infant in whom

TABLE 2.—*Comparison of Present Data with Those of Rominger and Meyer*

Infant	Age, Weeks	Length of Period, Days	Sodium Chloride + Potassium Chloride, Gm. per Day	Sodium Chloride + Potassium Chloride (Rominger) Gm. per Day	Length of Period, Days	Age, Weeks	Infant
O. II	11	6	0.07	0.13	5	13	S. I
D. I	14	6	0.17				
D. II	16	6	0.18	0.22	21	17	S. II
M. I	16	6	0.19				
Mo. III	28	6	0.16	0.175	3	30	R. I

TABLE 3.—*Daily Retention of Minerals of Infant on Cow's Milk Corrected for Loss Through the Skin*

Mineral	Age of Infant, Months	Retention, Millimols	Excretion Through the Skin, Millimols	Percentage Excreted Through the Skin	Corrected Retention, Millimols	Uncorrected Retention of Infant on Breast Milk, Millimols
Sodium	3	4.87	0.66	13.5	4.21	2.53
Potassium	3	4.56	1.75	38.4	2.82	2.50
Chlorine	3	4.84	0.88	18.2	2.96	2.02
Sodium	6	5.62	0.50	8.9	5.12	2.24
Potassium	6	5.19	1.54	29.7	3.65	2.42
Chlorine	6	6.08	0.78	12.8	5.30	2.00

the corrected retentions of potassium and chlorine are still much greater than those of the breast-fed infant. The table also indicates the percentage of loss through the skin to be expected for potassium, chlorine and sodium.

COMMENT

It is apparent from our data that no metabolic experiment involving retention of minerals can be correctly evaluated unless loss through the skin is determined. Especially must this fact be emphasized in respect to potassium. Another fact that should be emphasized is the excess of basic elements in the sweat. It may be seen from our data that chlorine, the main acid element, neutralizes less than one-half the determined fixed base.

We are extending our work and soon hope to have data on the loss of minerals through the skin of the breast-fed infant.

SUMMARY

1. The loss of minerals through the skin of infants for six day periods is reported.

2. The loss of potassium through the skin varies between 30 and 38 per cent of the calculated retention.

3. Chlorine and sodium are excreted to a lesser extent, but the amounts are considerable, while the loss of calcium and phosphorus through the skin may be considered negligible.

Case Reports

ABSCESS OF THE BRAIN FOLLOWING ACUTE OSTEOMYELITIS OF THE SUPERIOR MAXILLA

I. J. WOLF, M.D.
PATERSON, N. J.

A case of acute osteomyelitis of the superior maxilla, occurring in an infant, complicated by a cerebral abscess of the frontal lobe is reported.

REPORT OF CASE

Lawrence G., aged 5 days, was admitted to the Buffalo Children's Hospital on June 21, 1929, for the treatment of infected forceps wounds. The patient was the result of a full term, first pregnancy, and was delivered with difficulty. Examination showed a well nourished infant with two deep, infected lesions, one on each side of the face, in the region of the ear. There was a right-sided facial paralysis.

The temperature was normal throughout, except for an occasional rise to 100 F. Cultures from the wounds on the head revealed a few diphtheroids and staphylococci. The wounds healed uneventfully on treatment with wet dressings and irrigations. The patient was discharged on July 16, weighing 9 pounds (4,082.33 Gm.).

Second Admission.—On July 29, the baby was examined in the clinic because of a discharge from the left ear of two days' standing. On August 5, both ears were discharging pus. The patient was readmitted on September 27.

Examination revealed an infant aged 3 months with scars on the face from an instrumental delivery. The right eyelids were red and swollen so that the eye could not be seen. The conjunctiva was edematous but clear. There was a thin discharge from the nose. The breath sounds were roughened in the upper lobe of the right lung.

Course.—On September 29, an abscess below the right inner canthus opened spontaneously and discharged pus. It was treated with wet dressings, and continued to drain abundantly. The lower lid, still swollen and red, was incised two days later, but no pus was obtained. On the right side of the upper gum, at the point of the lateral incisor tooth, a sinus draining pus was discovered. The next day a small amount of blood and pus was draining from the right nostril; moderate drainage came from the sinus at the canthus. Cultures from the latter revealed Staphylococcus aureus. Roentgenograms of the nasal sinuses were indeterminate. Diarrhea and excoriation of the buttocks developed. During the first four days of this admission, the temperature ranged between 101 and 103 F., and then subsided gradually to normal. Examination of the blood showed 75 per cent hemoglobin, 12,000 leukocytes and 77 per cent polymorpho-

From the Buffalo Children's Hospital.

nuclears. On October 14, a direct transfusion of 160 cc. of blood was given. The swelling of the right periorbital tissues subsided quickly. The sinus in the gum remained. The patient was discharged improved.

Third Admission.—Discharged from the hospital on November 8, the patient was well until November 19, when he had three convulsions. On November 24, he became cross and fretful and slept poorly, and a few days later loose green stools developed. He had frequent attacks of screaming, and the respirations became rapid and difficult. He was readmitted to the Children's Hospital on November 27.

Examination.—The patient was an anemic infant of 5½ months, weighing 11 pounds (4,989.5 Gm.). There was marked asymmetry of the skull and face. The respirations were rapid and labored. The pupils reacted sluggishly to light; otherwise neurologic signs were absent. The ear-drums were normal. There were slightly diminished resonance in the left side of the chest posteriorly and numerous râles at the bases of the lungs and in the axillae. The liver was slightly palpable. The temperature on admission was 106 F. The respiratory rate was between 60 and 80 per minute. The blood showed 75 per cent hemoglobin, 14,900 white cells and 58 per cent polymorphonuclears. The infant died on November 30, three days after admission.

Autopsy (Dr. A. G. Foord, Buffalo General Hospital).—The body was that of an anemic boy aged 5½ months. There were no erupted teeth, but a small sinus was present in the upper part of the right jaw just above the usual site of eruption of the canine tooth. The head was considerably asymmetrical. There was very little occiput, and the cranium bulged more to the right than to the left. A slight thickening of the costochondral junctions and also of the bones of the ankles and wrist was felt. Microscopically there was evidence of rickets. The skull showed craniotabes. There was a healed scar, 2 inches (5 cm.) long, anterior to the left ear.

When the head was opened, the skull cap was poorly ossified, and the dura was markedly adherent to the bone along all the suture lines. The longitudinal sinus was thrombosed throughout its entire extent by a firm gray thrombus. This process extended down the right transverse sinus. The other sinuses were free. The dura was loosely adherent to the leptomeninges over the entire right frontal lobe and to some extent over the upper portion of the tip of the temporal lobe.

On reflection of the brain there was found a small pocket of pus on the inferior surface of the right frontal lobe, covering the posterior portion of the cribriform plate of the ethmoid. The brain tissue was extremely thin over this area, and pus exuded from a small opening in the anterior portion. The entire tip of the frontal lobe was fluctuant, and on section a large abscess filled with thick pus was found. This involved particularly the inferior part of the lobe, and extended backward, compressing the anterior portion of the internal capsule. The anterior horn of the right lateral ventricle was also encroached on.

The abscess was 4.5 cm. long and 2.5 cm. wide and was surrounded by a wall 1 mm. thick. The surrounding brain tissue was moist, but no hemorrhage was seen. Two small areas of hemorrhage were seen in the opposite frontal lobe. In the latter the small blood vessels leading to the superior sagittal sinus were thrombosed.

The leptomeninges at the base showed a purulent exudate. The rest of the surface of the brain showed diffuse hyperemia. Gross sections revealed nothing further of interest. Smears from the abscess showed gram-positive cocci, mostly

clumped and paired; the meninges showed moderate numbers of staphylococci and small gram-positive cocci in pairs and short chains.

The bone under the involved portion of the right frontal lobe was very rough when the dura was reflected. Dissection through the ethmoid region showed no cells, but an increase of diffuse connective tissue. The sphenoid sinus was normal. The right antrum showed some granulation tissue in the wall, but no pus. The right middle ear contained a thin mucous secretion; the left middle ear, antrum and mastoid were filled with greenish pus. Smears from the latter revealed a variety of organisms, a gram-positive diplococcus or short bacillus predominating.

The adenoid tissue in the nasopharynx was slightly hypertrophied. The thyroid was free from change. Both pleurae showed a very thin tenacious exudate, with fibrin over the bases. The dependent portions of the lungs were moderately boggy, and some areas were consolidated. Pus exuded from all the bronchial tubes. The myocardium was slightly paler and flabbier than normal.

The abdominal cavity was normal. There was moderate edema of the mucosa of the entire colon, whereas the rest of the gastro-intestinal tract showed nothing except anemia of the mucosa. The spleen was slightly enlarged. The liver was paler than normal and bulged under the capsule. The striations were somewhat obscured. The suprarenals, pancreas, bladder and genitalia were normal.

The pathologic diagnosis was: chronic brain abscess in the right frontal lobe with surrounding edema of the brain; chronic meningitis with adhesions of the dura over the right anterior half of the brain; recent purulent leptomeninigitis; old thrombosis of the superior sagittal sinus and the right transverse sinus; chronic right antral sinusitis and residue of an old ethmoiditis; left-sided otitis media and mastoiditis; hypostatic hyperemia, edema and bronchopneumonia in the lower lobes of both lungs with fresh serofibrinous pleurisy; cloudy swelling of the heart and kidneys; hyperemia of the liver; slight rickets; asymmetry of the skull, and a linear scar anterior to the left ear.

REVIEW OF THE LITERATURE

Kelly,[1] who collected seventeen cases of osteomyelitis of the superior maxilla in infants, described the condition as "a disease characterized by redness and swelling below one eye, the formation of sinuses in this region and in the alveolus, and by a purulent discharge from the corresponding nostril. The superior maxilla is involved in an osteomyelitis process, and evidence of the disease is presented by each of its bony surfaces—the orbital, nasal, facial and palatal."

As in all osteomyelitic processes, the acute stage is followed by a chronic one. Sequestrums and teeth are usually discharged from the alveolar sinuses. A mucopurulent discharge persists, usually from the nose, intermittently for from weeks to years. When a rudimentary tooth is extruded from the alveolar sinus, it fails to appear later in the affected part of the maxilla. The permanent tooth may appear as a deformed stump following the extrusion of the temporary one, and be

1. Kelly, A. B.: The So-called "Empyema of the Antrum of Highmore in Infants" (Osteomyelitis of the Superior Maxilla), Edinburgh M. J. **16**:302, 1904.

extruded itself later. Röpke,[2] in his case, reported the affected side of the face to have become slightly sunken.

The etiology of this disease cannot be discussed here, but has been adequately considered by Kelly and by Terracol,[3] and in the American literature by Bass [4] and by Wilensky.[5] Concomitant conditions may exist, in which a clue to the etiology has been sought. Thus gonorrheal conjunctivitis may appear following birth, and a week later the clinical picture described.[6] Avellis [7] found tubercle bacilli in the nasal discharge when the infant in his case was 15 months old; the onset of the illness was at about 6 weeks of age. The infant may have been syphilitic.

Complications.—Septicemia and pyemia are not rare. Zarfl [8] described two cases that came to autopsy in which the histologic picture was that of sepsis.

A fatal case of D'Arcy Power's [9] showed pleurisy, bronchopneumonia, pericarditis and an abscess in the right lung at autopsy. The superior maxilla was extensively necrosed and contained two sequestrums. The infant had been delivered by forceps; the onset of symptoms was at the age of 1 month. Death occurred at the age of 8 weeks following an operation to enlarge the canthal sinus. An opening was made through the floor of the antrum in order to pass a drainage tube from the mouth to the eyelid.

An abscess of the brain was reported by Collet.[10] A primipara's infant took sick on February 26, with coryza, conjunctivitis and anorexia. This was followed by a serous discharge from the left side of the nose and edema of the left eyelids. An alveolar sinus appeared, and the nasal discharge became thick and purulent. Bacteriologic examination of the secretions of the nose and mouth revealed staphylococci. On March 6, there were two sinuses in the mouth from which teeth and spicules of bone were extruded after probing. The infant was discharged on April 12, improved; it returned to the hospital on

2. Röpke, quoted by Kelly (footnote 1).

3. Terracol, J.: L'ostéomyélite du maxillaire supérieur chez le nourrisson, Arch. internat. de laryng. **34**:532 (May) 1928.

4. Bass, M. H.: Acute Osteomyelitis of the Superior Maxilla in Young Infants, Am. J. Dis. Child. **35**:65 (Jan.) 1928.

5. Wilensky, A. O.: The Pathogenesis and Treatment of Acute Osteomyelitis of the Jaws in Nurslings and in Infants, Am. J. Dis. Child. **43**:431 (Feb.) 1932.

6. Bouchert, quoted by Kelly (footnote 1).

7. Avellis, quoted by Kelly (footnote 1).

8. Zarfl, quoted by Bass (footnote 4).

9. Power, D'Arcy, quoted by Terracol (footnote 3), Collet (footnote 10) and Kelly(footnote 1).

10. Collet, F. J.: Sinusite maxillaire du nouveau-né, Arch. internat. de laryng. **28**:1041, 1922.

May 25, with meningitis. At autopsy, the right lateral ventricle was distended with pus, and the left ventricle contained serous fluid. The site of the abscess was not mentioned in the report except that the author pointed out that it was situated on the opposite side to that of the "sinusitis." He believed that both occurred simultaneously with the inception of a septicemia, although the abscess of the brain was latent in appearance, as is commonly seen.

Abscesses of the extremities were reported by Lemaître [11] and by Roure.[12] In the latter's case, the abscesses to which the infant succumbed formed on the forearm and on the foot. The mother had suffered from metritis and septic vaginitis during the last months of pregnancy.

An abscess of the left breast in a 2 weeks old infant was reported by Bertèmes.[13] Staphylococci were recovered from it as well as from the osteomyelitis of the maxilla. The patient recovered.

Bloch and Lemoine [14] encountered a superficial abscess of the scalp and a deeper one at the level of the temporal fossa, complicating an osteomyelitis of the maxilla. Their patient also recovered.

Fürst [15] reported the case of an infant, aged 5 weeks, who died. Autopsy showed necrosis of the entire upper part of the right jaw; abscesses were found beneath the zygomatic process of the frontal bone and among the fibers of the temporalis muscle. Multiple abscesses were present in both lungs, kidneys, etc., as well as purulent pleurisy and pericarditis.

Guisez [16] reported a case in an infant, aged 6 months, complicated by thrombosis of the ophthalmic vein and of the cavernous sinus.

Recently, Roehm [17] reported a case of acute osteomyelitis of the maxilla in an infant 5 months old, complicated by bilateral parotitis on the fifteenth day of the illness. An abscess formed on the right side, which was incised and drained. Roentgen examination showed disappearance of the right nasal bone and of the whole lower half of the orbit. A month and a half after the onset of the illness, a persistent cough developed, with the production of a great quantity of

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11. Lemaître, quoted by Terracol (footnote 3).

12. Roure, M.: Ostéo-périostite maxillaire et orbitaire chez un nouveau-né; généralisation; mort, Arch. internat. de laryng. **11**:137, 1898.

13. Bertèmes: L'ostéomyélite du maxillaire supérieur chez le nourrisson, Ann. d. mal. de l'oreille, du larynx **46**:587 (June) 1927.

14. Bloch, A., and Lemoine, J.: A propos de la fausse sinusite du nourrisson, Arch. internat. de laryng. **34**:192 (Feb.) 1928.

15. Fürst, quoted by Kelly (footnote 1).

16. Guisez: Thrombo-phlébite du sinus caverneux, Rev. de stomatol. **17**: 469, 1912.

17. Roehm, H.: Acute Osteomyelitis of the Superior Maxilla in a Young Infant, Am. J. Dis. Child. **42**:1171 (Nov.) 1931.

mucus. A roentgenogram of the chest revealed multiple areas of emphysema, combined with small pneumonic areas.

COMMENT AND SUMMARY

A case of acute osteomyelitis of the superior maxilla, complicated by a cerebral abscess of the frontal lobe is reported. The infant was a first-born child and had sustained forceps wounds at birth which became infected.

Complications are not uncommon in osteomyelitis of the maxilla in infants. Many of these favor an osteomyelitic etiology of the disease. A positive blood culture may be obtained, and death may result from the septicemia or pyemia. Pyemic abscesses have been reported in the brain, lungs, kidneys and other visceral organs. They may also form in the extremities, the breasts and the scalp. In the case of abscess of the brain reported by Collet the condition was probably metastatic; the abscess in my case was probably spread by direct extension, as indicated by the postmortem observations. Similarly, in Roehm's case the nasal and orbital bones were involved by direct extension.

It is now accepted that the clinical entity described is osteomyelitis of the maxilla rather than maxillary sinusitis. The causative organism is usually Staphylococcus aureus. At the age at which this disease manifests itself the sinuses are too small to cause this syndrome. On roentgenologic examination, the sinuses are indeterminate.

Treatment should be simple and conservative, favoring drainage and the opening of abscesses as they point. Operative intervention is often fatal, or may result in disfiguring scars.

400 Broadway.

ARGYRIA FROM THE USE OF COLLOIDAL SILVER IODIDE INTRANASALLY

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Argyria due to the administration of silver salts is by no means rare; a careful review of the literature, however, has failed to reveal mention of the condition as a result of colloidal silver used intranasally.

Because of the widespread use of this type of medication and the importance of prevention of this irremedial disfigurement, I deem these cases worthy of report.

CASE 1.—*History.*—B. V., a girl, aged 7 years, an only child of well educated, middle-aged parents, was brought to me because of the peculiar color of the skin of her face and hands.

She had been normally delivered at full term, and had been breast fed and bottle fed on Mellins' food under the direction of a local physician. She had always been overweight, but was normal except for a poor appetite. Too much attention from mother and grandmother was evident, the feeding history being typical of the one-child type. Scarlet fever occurred at 3 years, and pertussis at 4 years. She had recurrent tonsillitis and colds, with occasional gastro-intestinal disturbances. The peculiar color of the skin was first noticed about two years before I saw her. A few months later, the child's tonsils were removed to improve her appetite and because she had poor color. The doctor had asked the mother at that time if the child had been a blue baby at birth. Instead of the child's color improving after the tonsils and adenoids were removed, it had gradually grown worse. Recently the child had been taken through two clinics for careful examination, and each report was entirely negative. No diagnosis had been suggested.

Careful inquiry into the medication that the child had received revealed the fact that no medicine had been given either by mouth or by rectum. The mother casually mentioned that the child was thoroughly cooperative and would permit, without objection, the instillation of neo-silvol into her nostrils. When asked how much and how often neo-silvol was used, the mother said one-half a medicine dropper had been instilled in each nostril, night and morning, for the past four years. She stated further that her physician had first written the prescription for a cold and sore throat, and that they had had such excellent results that she had decided to use the preparation to prevent colds and other diseases. She had not consulted the physician, but obtained the name and percentage strength of the neo-silvol and ordered it freshly prepared every second week from her druggist.

Physical Examination.—The child on first appearance was most startling because of the unusual color of her face and hands. The color is best described as that of a fairly light Negro who has had a sudden pallor from fright or illness. It was nearer slate than any other color. Her conjunctivae were a grayish

yellow, and her lips resembled those of a child with congenital heart disease. The area of skin around the nose and mouth was somewhat lighter. Her hands and wrists were darker than normal, and her finger-nails were the color of those seen immediately after death. The body surface which had not been exposed to sunlight showed no change from normal.

The results of a general physical examination were entirely negative. Her height was 48 in. (122 cm.) and her weight 58 pounds (26,300 Gm.). Her tonsils and adenoids had been removed. The eyes were normal, except for discoloration of the sclera. Nose, throat and ears were normal. Heart, chest, abdomen, genito-urinary tract, bones and joints and reflexes were normal.

Laboratory Examination.—The urine was yellow, acid and clear. The specific gravity was 1.02. There was no albumin or sugar. A few squamous cells, a few mucus threads and an average of 10 pus cells to the low power field were present. The red blood cells numbered 4,390,000; the white cells, 8,400; hemoglobin, 84 per cent. The differential count showed: polymorphous neutrophils, 56 per cent; lymphocytes, 40 per cent; large mononuclears, 2 per cent, and eosinophils, 2 per cent. The blood was negative for plasmodia, and the stool was negative for parasites.

Progress.—One year has elapsed since the diagnosis was made, and there is no change in the child's color.

Case 2.—*History.*—B. E. C., a boy, aged 5 years, was brought to me from a neighboring town. He was the only living child of well educated, middle-aged parents, and had been under my care since 3 months of age. One sister died of acute dysentery when 9 months old, about one year before the birth of this child. The mother had not reacted well to this shock, and nervous apprehension was evident. According to her physician, the mother had an arrested case of tuberculosis, and a brief conversation with her was sufficient to warrant a diagnosis of definite psychoneurosis, especially in regard to the child.

This child had a normal birth, at full term, and breast feeding was attempted. I first saw him at 3 months of age, when the complaints were colic, failure to gain weight, mucous stools and crying. With the administration of a suitable formula and the omission of daily doses of castor oil and castoria, the baby became a perfectly normal infant. Recurring tonsillitis began at 1 year and continued periodically until he was brought to me for examination about ten months prior to the present writing. The complaint at that time was an afternoon elevation of temperature to 100 degrees and poor color. On further investigation into the history it developed that the mother had called me on the long distance telephone and asked what to do for a beginning cold and sore throat in the child when he was about 18 months of age. Because a prescription would have meant a delay, I foolishly told her to order one-half ounce (14.175 Gm.) of 10 per cent neo-silvol and to drop 5 drops in each nostril every four hours. She was so pleased with the result that she continued to use neo-silvol as a preventive measure without my knowledge. She had used the preparation night and morning two or three days a week for the past three years.

Physical Examination.—The child's appearance was that of a well nourished, well developed child. His height was 44 inches (111.76 cm.), and his weight, 48 pounds (21,800 Gm.). His complexion, however, suggested poor health. On closer observation there was a greenish-gray tint to the face, especially noticeable around the mouth and nose. Because the child was a decided blond, the change in color was more evident. His sclera resembled that of mild jaundice, except

for a grayish tint. He had hypertrophied, chronically inflamed tonsils and adenoids with cervical adenitis. The chest was normal except for a positive D'Espines sign, with confirmation of tracheobronchial lymphadenitis by roentgenogram. There was slight evidence of Harrison's groove. The heart was normal in size and rhythm, with a rate of 108 per minute. The abdomen, the genito-urinary tract and the osseous and nervous systems were normal. The Moro and Mantoux tuberculin reactions were both positive.

Laboratory Examination.—The urine was yellow, acid and clear, with a specific gravity of 1.016; it contained no albumin or sugar, a few squamous cells and only occasional pus cells. The blood count was: red cells, 4,320,000; white cells, 7,800; hemoglobin, 85 per cent; color index, 0.9. Examination of the stool gave negative results. The blood was negative for plasmodia.

The diagnosis was tuberculous tracheobronchial lymphadenitis, hypertrophied and chronically inflamed tonsils and adenoids and incipient argyria.

Progress.—Tonsillectomy and adenoidectomy were done, and the child was placed on the regimen used for tuberculous patients, with omission of neo-silvol. At the present time he is in excellent health, the temperature is normal, and the tracheobronchial lymph nodes are less enlarged. His color is unchanged, but this is not conspicuous, owing to the early diagnosis and omission of neo-silvol.

CASE 3.—*History.*—J. R., a boy, aged 8 years, is the only child of a physician in a neighboring state. The child was seen by chance in the rooms of the American Medical Association of Vienna, November, 1931, while his father and I were doing postgraduate work there. Because of the child's unusual color and because I had seen the cases already referred to, I talked with the father about the child's condition. He gave the following history:

At 2 years of age, the child had acute otitis media followed by a tonsillectomy. At that time an otolaryngologist advised the use of neo-silvol intranasally for prevention and treatment of coryza. Measles and chickenpox had both occurred since then, with no complications. Like most physicians, he paid very little attention to the medical situation in his own home, but he remembered that the mother had dropped about half a dropper of neo-silvol in each of the boy's nostrils three times a week during the winter as a preventive measure, and every two hours during acute attacks of coryza. This had been continued for the past six years. About a year and a half before I saw the child they first noticed the discoloration of his face. The child had been examined by competent pediatricians in Kansas City and New York and, recently, in Vienna. None of them had suggested a diagnosis except the Viennese pediatrician, who suggested the possibility of the peripheral blood vessels being situated more deeply than usual. The results of examination of the blood on Oct. 15, 1931, in Vienna, were as follows: red cells, 4,780,000; white cells, 8,400; color index, 0.9; hemoglobin, 85 per cent.

The physical examination was not made by me, but at that time the results were entirely negative according to the report of the pediatrician who had recently examined the child.

SUMMARY

1. Three cases of argyria in children from excessively prolonged use of neo-silvol intranasally are reported.

2. All the cases occurred in well-to-do, one-child families with overanxious mothers.

3. The neo-silvol in each case was purchased in 10 per cent strength by the mothers direct from the druggist, without a physician's prescription after the first time.

CONCLUSION

When colloidal silver salts are prescribed for intranasal use, the mother should be warned against continuing such medication over too long a period, and druggists should not dispense such products without a physician's prescription.

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SPONTANEOUS PNEUMOTHORAX IN THE NEW-BORN

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AND
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Judging from the published reports, pneumothorax in the new-born is rare. In a recent article, Stein [1] described a case of pneumothorax in an infant and, after "an exhaustive review of the literature in all languages indexed at the New York medical libraries," was able to find only four previous instances. Stein's patient presented evidences of a right-sided penumothorax, first noted at the age of 1 week. At the time the report was made the child was 2 years old and still gave typical physical and roentgenologic signs of air in the thoracic cavity. Cyanosis and dyspnea were at no time prominent. Ruge [2] recorded an instance of pneumothorax in a new-born infant in 1878. Autopsy showed an irregular tear of the pleura, 3 cm. long. Since birth occurred by breech presentation in this case, the author thought that the infant aspirated meconium during the delivery, which led to a circumscribed emphysema and later to a rupture of the visceral pleura. Scheltema [3] reported the occurrence of air in the chest of a baby of 7 weeks who presented the clinical and roentgenologic evidences of a left-sided pneumothorax. At the age of 3 months, the change persisted, but the infant's condition was satisfactory. Smith,[4] in 1919, also reported a case of left-sided pneumothorax in a 7 months old baby. Bronchopneumonia developed soon after the infant's entrance to the hospital, and the patient died a short time later. No autopsy observations were submitted. Flipse [5] published a report of a

From the departments of pediatrics and medicine of the University of Illinois College of Medicine and the University Hospital.

1. Stein, J.: Congenital Pneumothorax, Am. J. Dis. Child. **40**:89 (July) 1930.

2. Ruge, C.: Pneumothorax bei einem Neugeborenen, Ztschr. f. Geburtsh. u. Gynäk. **2**:31, 1878.

3. Scheltema, quoted by Stein (footnote 1).

4. Smith, C. H.: Complete Pneumothorax, Arch. Pediat. **36**:184, 1919.

5. Flipse, M. J.: Pneumothorax in Newborn Infant, J. Florida M. A. **14**:403, 1928.

case of pneumothorax in which the infant, when born, made no attempt to breathe until after a tracheal catheter was inserted. The presence of cyanosis and the physical and roentgenologic findings established the diagnosis of air in the pleural space. With a syringe 30 cc. of air was withdrawn from the left side of the thorax, and later another 18 cc. At the time of the report the baby's condition was satisfactory. Flipse was of the opinion that the lack of adequate respiratory movements at birth was due to collapse of the epiglottis, and that efforts at initiating respiration caused a rupture of the lung.

In addition to the four cases collected by Stein and a fifth one reported by him, there are two recorded by Weiner [6] whose publication appeared also in 1930. The first case was that of a baby 4½ months of age in whom there developed a phlegmon of the buttocks, septicemia and bilateral pneumothorax. Autopsy was not permitted. The second infant was first seen by Weiner at the age of 5 weeks at which time it suffered with intermittent attacks of cyanosis and presented physical signs of a partial left-sided pneumothorax. The child died at the age of 4½ months. Autopsy disclosed a communication between a branch of the upper part of the left bronchus and the pleural cavity. Another example of pneumothorax in the new-born was recently observed by us. On account of the rarity of the condition and because of the nature of the causative lesion a detailed account seems warranted.

REPORT OF CASE

E. S., 3 weeks of age, was brought to our office on July 27, 1931, by the mother, on account of moaning and fever which were observed during the five hours preceding the visit. The mother stated that the baby had breathed peculiarly since birth and cried almost incessantly. The patient, who was the second child, was delivered spontaneously after a labor of three and one-half hours. Its birth weight was 7 pounds and 11 ounces (3,486.98 Gm.), which, after ten days dropped to 7 pounds and 10¼ ounces (3,465.73 Gm.). The essential observations noted on July 27, 1931, were as follows: The infant appeared well nourished and weighed 8 pounds and 12 ounces (3,968.94 Gm.). The pulse rate was from 145 to 150 per minute. Respirations numbered 40 per minute and were accompanied by dilatation of the alae nasi and an expiratory grunt. The temperature was 103.8 F. There was hyperresonance over the entire right side with absence of breath sounds, except along the hilus where many fine crepitant râles were heard. The heart was displaced to the left side, the apex being in the fourth interspace in the midaxillary line. No murmurs were heard.

6. Weiner, C.: Spontanpneumothorax beim Säugling, Arch. f. Kinderh. **91**: 14, 1930.

The results of roentgen examination (fig. 1, *A*) which confirmed the diagnosis of pneumothorax were reported as follows: "The right lung is collapsed, partially and evenly. There is no evidence of fluid. The heart and mediastinum are pushed to the left. The collapsed lung appears to be completely atelectatic. No evident cause is noted in this film." The presence of an associated pneumonia which was suspected clinically could not be determined roentgenologically. The cyanosis gradually progressed, the general condition grew worse, and aspiration of the air from the right side of the chest was decided on. About 25 cc. of air was withdrawn from the right side followed by an immediate clinical improvement. Another roentgenogram (fig. 1, *B*) taken within half an hour after aspiration showed a decrease in the air content of the right side of the pleural cavity. The

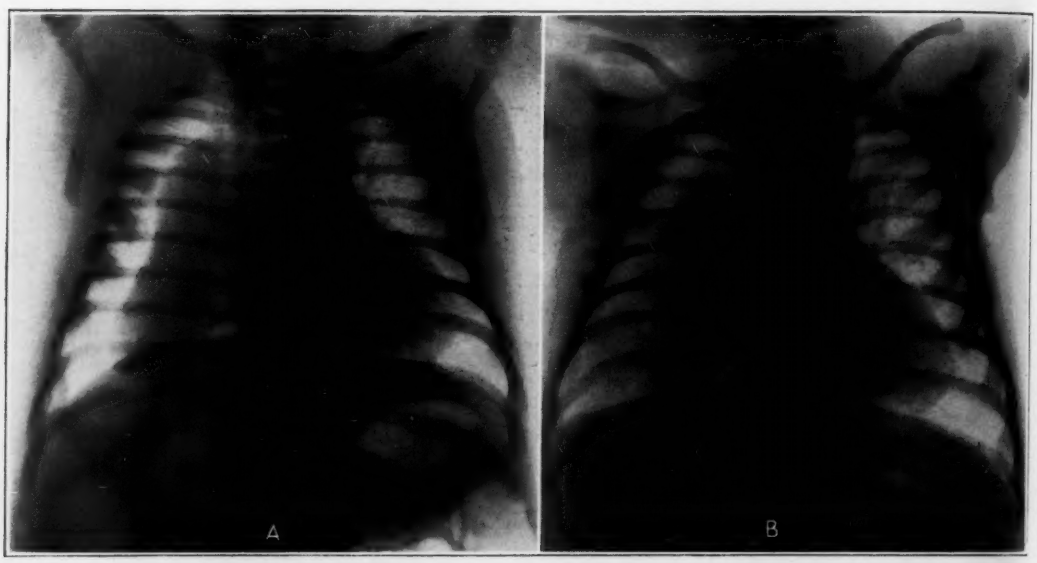

Fig. 1.—*A*, spontaneous, right-sided pneumothorax with displacement of the heart and mediastinum to the left. *B*, appearance of the chest one-half hour following aspiration from the right pleural cavity of 25 cc. of air. The heart and mediastinum have practically returned to their normal positions. The right lung is still relatively airless.

lung was still airless. The improvement, however, was of very short duration, and the baby died on July 30, 1931, three days after the onset of acute symptoms.

Postmortem Report.—Autopsy was performed shortly after the death of the infant. External examination showed the right side of the thorax to be distended and the intercostal spaces widened. There was diffuse cyanosis of the skin and mucous membranes. The most significant changes internally were found in the chest. The mediastinal structures were displaced to the left, and the right diaphragmatic leaf was depressed. When the right pleural cavity was opened there was a gush of odorless gas. In the upper right posterior portion of the

thoracic cavity was the contracted lung, and in the dependent portion of the right side of the chest there was 200 cc. of a serofibrinopurulent exudate.

The right lung (fig. 2) was covered by a thick fibrinous membrane which was most prominent about the lower lobe (*b*). The posterior aspect of this lobe presented a defect (*a*) which measured 7 by 8 mm. The margins of this defect were irregular and serpiginous, and the floor was nodular and covered with fibrin. The base of the ulcer was 2 mm. below the pleural surface of the lobe. About this area for a distance of from 2 to 3 mm. the lung was unchanged except for a more or less uniform firmness and diminished air content.

The associated changes, which do not merit detailed description, were included in the anatomic diagnosis, which reads: "Defect of the right upper pulmonary lobe

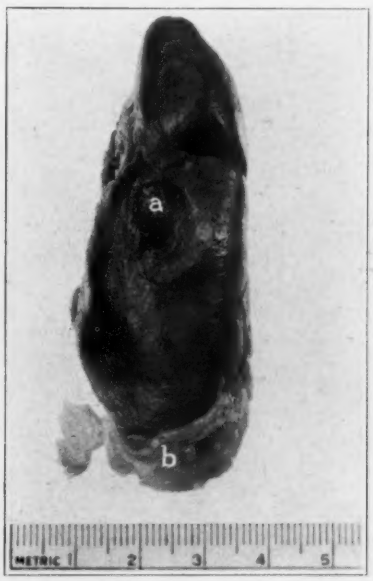

Fig. 2.—Photograph of the right lung viewed posteriorly. Near the apex of the lower lobe is an irregular defect (*a*) due to rupture of a subpleural abscess. The fibrinous exudate is best seen as a thick membrane (*b*) covering the base of the lung.

(following solitary sub-pleural abscess with perforation); right pnemothorax; diffuse right serofibrinopurulent pleuritis; compression atelectasis of the right lung; lateral displacement of the heart and mediastinum; downward displacement of the right leaf of the diaphragm and of the liver; blood-distended right auricle; generalized venous stasis; gas-distended intestines (paralytic ileus); cloudy swelling of the parenchymatous organs; focal hemorrhages (asphyxial) of the subepicardial and periaortic tissues; fatty changes of the liver; focal atelectasis and emphysema of the left lung."

Section for microscopic examination were taken through the site of perforation beyond the adjacent consolidated portion in order to include normal pulmonary

tissue. A series of changes which were arranged more or less in separate zones were encountered in passing from the inner portion to the periphery of the lung substance. The zone farthest from the pleural surface consisted of normal alveoli except for partial atelectasis and the presence of a few desquamated cells. The adjacent air sacs in passing peripherally were seen to contain in addition a few eosinophilic leukocytes. The next change noted (fig. 3, *a*) was obliteration of the alveolar spaces by young granulation tissue in which were numerous macrophages, round cells and eosinophilic leukocytes. In places the eosinophils were so numerous

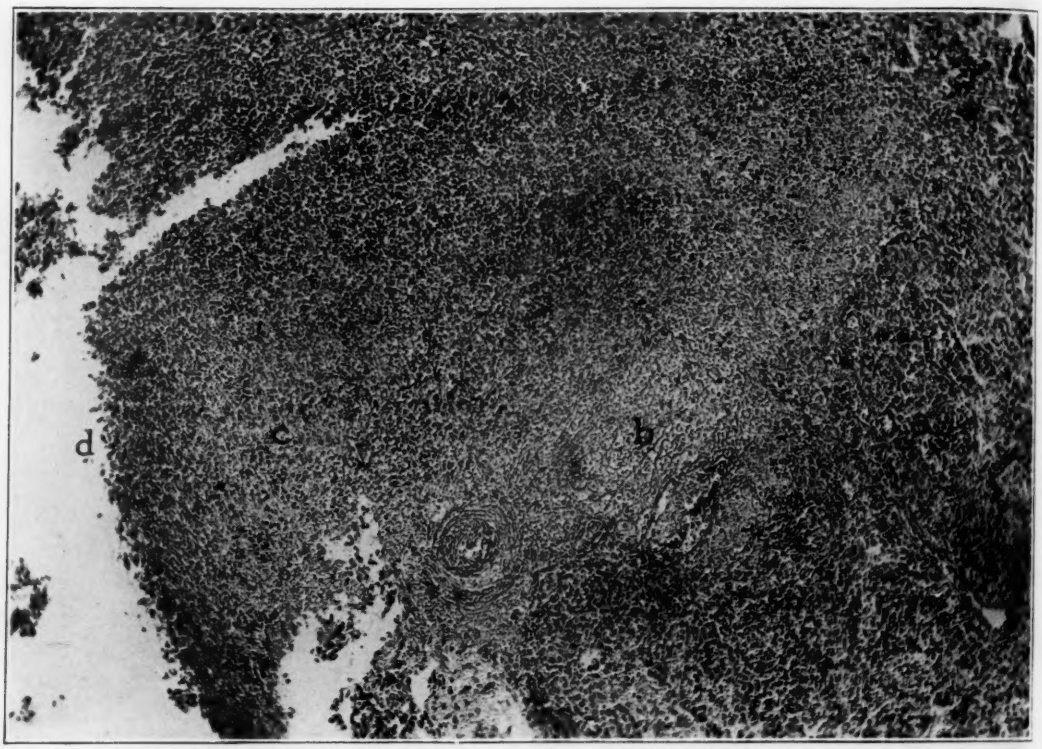

Fig. 3.—Photomicrograph of a section taken through the site of perforation to include the adjacent consolidated tissue. In passing centrifugally there are encountered successively zones of granulation tissue (*a*), fibrinoid necrosis (*b*) and cellular débris (*c*). The defective pleural surface (*d*) is ragged and irregular.

that more than 100 were collected in the ordinary high power field. Within some of the alveoli remnants of fibrin invaded by fibrocytes could be discerned. As the periphery of the lung was approached, there was found, bordering a defect, a thin zone of leukocytic infiltration. The latter was lined by an area of fibrinoid necrosis (fig. 3, *b*), and this in turn by a wide band rich in cellular débris (fig. 3, *c*). The surface of the mass of débris was irregular and lacked a pleural covering. Sections from various other portions of the lung demonstrated partial atelectasis and slight desquamation of the septal cells.

COMMENT

The pathogenesis of the process is somewhat conjectural. From the available evidence it seems likely that shortly following delivery the child aspirated some contaminated foreign material. This may have been in the form of saliva introduced through the catheter used by the obstetrician in clearing the infant's upper respiratory passages. The location of the infection at the apex of the upper lobe of the right lung in a child would favor a hypothesis of aspiration. The pneumonitis with its overlying pleurisy would explain the slight embarrassment to respiration and irritability that were noted from the time of birth until the acute symptoms supervened. The focus of pneumonitis or bronchopneumonia instead of resolving went on until formation of an abscess occurred. The abscess subsequently ruptured through the pleura, and thereby produced a communication between the lung and the thoracic cavity. The occurrence of the pneumothorax was associated with the acute onset of dyspnea and tachypnea. The subsequent development of fever and a serofibrinopurulent exudate was obviously due to the presence of viable organisms in the exudate that escaped from the ruptured abscess. Judging by their nature, the histologic changes were of the same age as the child (3 weeks). It is on this account that the infection is believed to date back to the time of the infant's birth.

SUMMARY

An example of pneumothorax in the new-born is presented, together with a review of the literature. The pathogenesis in the case described is somewhat conjectural. It is assumed that the primary factor was the introduction with the tracheal catheter of infected foreign material into the infant's respiratory tract immediately following delivery. The insufflated micro-organisms succeeded in producing a focus of bronchopneumonia which progressed to suppuration. Rupture of the softened bronchopneumonic focus led to escape of air into the thoracic cavity.

TOTAL UNILATERAL HYPERTROPHY

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NEW YORK

Reports of total unilateral hypertrophy or hemihypertrophy are comparatively rare in medical literature. The earliest case was reported by Wagner, in Germany, in 1839; in 1879, Osler gave the number of reported cases of congenital hemihypertrophy as twelve. Gesell, in 1921, made a careful search of the literature and collected forty cases, which included one of his own. In 1927, he was able to add thirteen to this number, making a total of fifty-three cases. Wiseberg and Halperin each reported a case in 1931. The present case is reported for two reasons: (1) because it presents an unusual anatomic anomaly, congenital in origin and (2) because the comparative rarity of the condition makes it seem worth while to add another case to the few recorded.

REPORT OF A CASE

The patient was a white girl, 3½ years of age, who first came to the pediatric clinic of the outpatient department in January, 1928; the mother complained that the child's right upper and lower extremities were enlarged. The family history revealed no similar conditions in the maternal or paternal branches of the family. The history of the preceding generations, as far back as the mother was aware, also failed to reveal any similar condition. The fact, however, that the patient's mother was one of twins may be of importance. This fact will be mentioned again in the discussion of the etiologic factors. The child was delivered spontaneously (cephalic presentation); the weight at birth was 8½ pounds (3,800 Gm.), and the developmental history was normal. The child had her first tooth at 4½ months and sat up at 5½ months. She had had none of the infectious diseases, and her health had been uniformly good.

The enlargement of the right upper and lower extremities was noticed by the nurse soon after delivery, and she called the mother's attention to it. Up to the time of the present writing the enlargement has persisted in about the proportion noticed at birth.

The physical examination revealed a fairly well nourished and well developed child, mentally alert and bright. The pupils were equal and regular and reacted to light and in accommodation. The right ear was definitely larger than the left, and the right side of the face fuller than the left. The right side of the chest and back was larger than the corresponding area on the left, and the right side of the vulva and buttocks was enlarged; the right upper and lower extremities were definitely enlarged from the shoulder to the fingers and from the hip to the toes.

From the Pediatric Department of the Hospital for Joint Diseases, New York, Service of Dr. Jacob Sobel.

Fig. 1.—Showing enlargement of the right lower extremity.

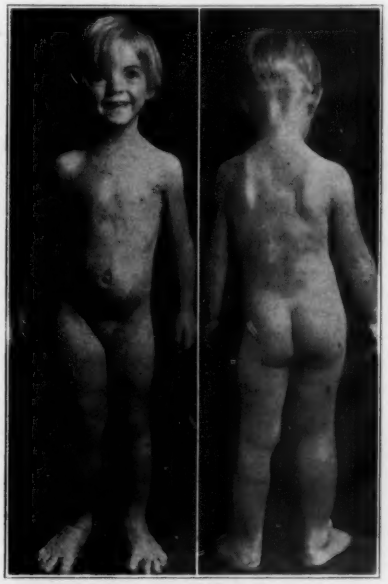

Fig. 2.—Showing hemihypertrophy of the right upper and lower extremities.

The entire chest and abdomen were covered with a purplish mottling which extended down to the left thigh. The back showed the same extensive mottling, and in the lumbosacral region there was a large, flat, port wine-colored nevus. The throat and teeth were normal. There was no adenopathy. The heart and lungs were normal. The abdomen was soft; the liver and spleen were not enlarged, and there were no masses.

The measurements of the upper extremities were: circumference of the right wrist, 12.5 cm.; the left wrist, 11.25 cm.; the right forearm, 16.25 cm.; the left forearm, 13.75 cm.; the right arm, 15 cm., and the left arm, 12.5 cm. The measurements of the lower extremities were: the circumference of the right thigh,

Fig. 3.—Showing hypertrophy of the right humerus and of the bones of the right forearm.

31.25 cm.; the left thigh, 26 cm.; the right calf, 26 cm.; the left calf, 21.25 cm.; the right ankle, 17.5 cm.; the left ankle, 15 cm.; the right foot, 20 cm., and the left foot, 17 cm. The circumference of the right side of the chest from the sternum to the spine was 26.25 cm.; of the left side of the chest from the sternum to the spine, 23 cm.

Roentgenographic studies were made by Dr. M. Pomeranz of the x-ray division. Comparison of figures 3 and 4 clearly shows the difference in width between the two humeri and between the bones of the respective forearms. The osseous hypertrophy is also shown in the bones of the hand. In the lower extremities, as shown

in figures 5 and 6, the relative hypertrophy of the right and left bony structures is clearly indicated. The roentgenograms, therefore, reveal complete hypertrophy in which both the soft tissues and the bones participate.

The laboratory data were all within normal limits: red blood cells, 3,680,000; leukocytes, 9,700; hemoglobin, 75 per cent; polymorphonuclear leukocytes, 25 per cent; small lymphocytes, 72 per cent, and large lymphocytes, 1 per cent. The bleeding time was three minutes and the coagulation time four minutes. The blood phosphorus was 5.3 mg. per hundred cubic centimeters of blood, and the blood calcium, 10.3 mg. The Wassermann test of the blood was negative.

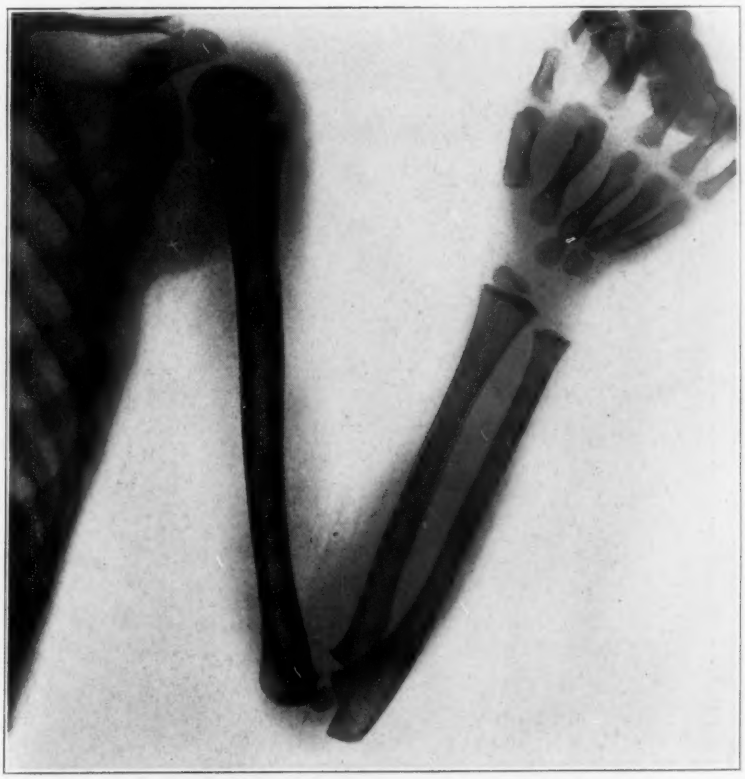

Fig. 4.—Showing hypertrophy of the left humerus and of the bones of the left forearm.

Gesell, in 1921, reviewed all the cases of hemihypertrophy then available in the literature. It is an interesting coincidence that of these forty cases, twenty-seven, or nearly 70 per cent, showed right-sided enlargements and that nineteen, or nearly 50 per cent, showed some cutaneous abnormalities. Associated with the enlargement was a high incidence of mental impairment, 13 per cent of the forty cases showing mental involvement ranging from slight aberration to idiocy.

In discussing the etiologic factors involved in the production of hemihypertrophy, one is confronted with conflicting opinions. The causes ascribed are various: 1. One group of authors ascribes the stimulation. 3. The inevitable explanation of the internal secretionists,

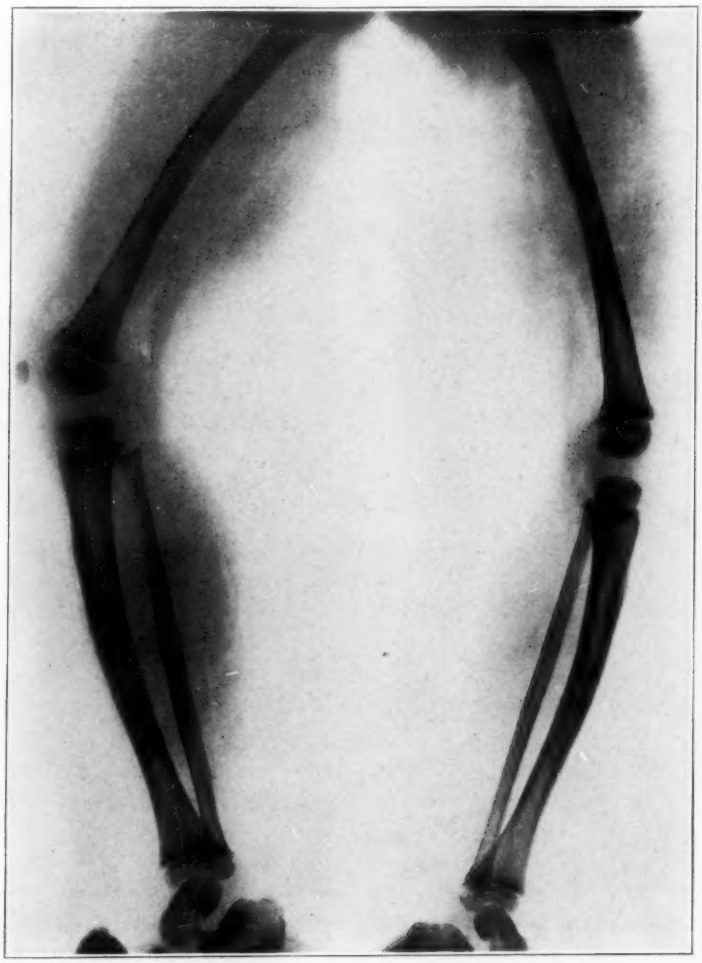

Fig. 5.—Showing the relative hypertrophy of the right bony structures over the left, knees flexed.

blood supply to the corresponding side, and in support of this theory cites the frequent occurrence of nevi and telangiectases. But no attempt is made to explain the root or cause of this vascular anomaly other than to hint at the possibility of heredity. There is, however, no evidence that hemihypertrophy is hereditary. In none of the known cases

was there an instance in which two members of the same or related families presented hypertrophy. 2. Wieland regards the cause as the stimulation of some of the embryonic somites to overgrowth. But here, too, he is silent as to the exact nature of the stimulus or of the means of

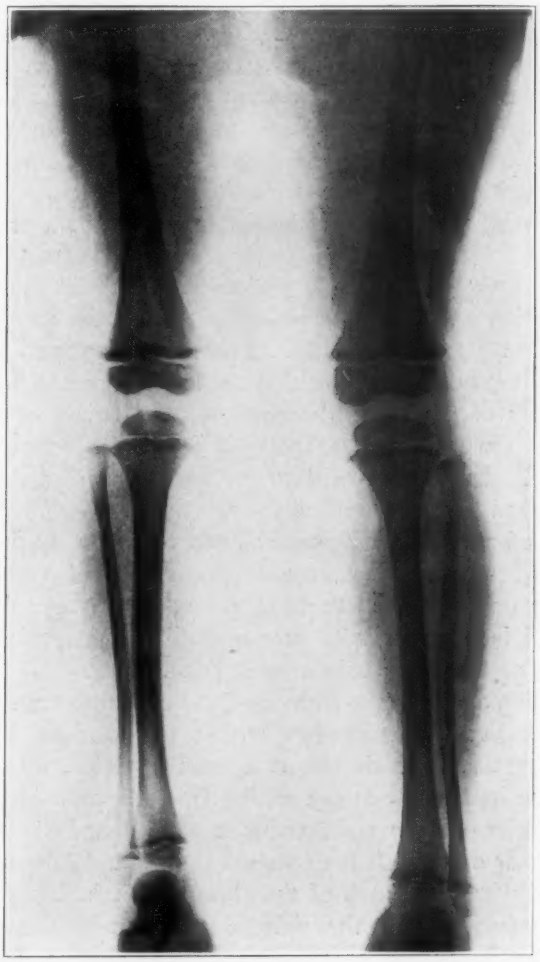

Fig. 6.—Showing the relative hypertrophy of the right bony structures over the left, knees straight.

stimulation. 3. The inevitable explanation of the internal secretionists, who hold the hypertrophy to be due to a biochemical reaction causing an irregular distribution of fetal tissues that interferes with the normal glandular secretions of the body, is propounded. 4. Finally, the subject of twinning has been given much prominence in an attempt to

explain the one-sided enlargement. The origin of duplicities has always been most difficult to explain, and the many attempted answers have been replete with conjectures.

Among the theories that have been formulated, the fusion theory of Marchand and Ziegler stands out most clearly. According to these workers, there are present two originally distinct anlagen within a single ovum. These two anlagen may develop separately and independently to produce twins. They may come into contact during development and fuse to a greater or lesser degree, thus producing some kind of duplicate monster. If fusion does occur, it occurs between similar parts of the two anlagen; in other words, like tissues and organs fuse—liver with liver, muscle with muscle, bone with bone, and so on. Such unions, however, probably occur only in the extremely early stages of development, for when tissues are once formed, union is effected with much greater difficulty. Consequently, fusion between two anlagen leading to the formation of a monster probably takes place at an extremely early period of intra-uterine life. From this explanation, which is based on much experimental work on the lower forms of life, one may conceive hemihypertrophy as the result of the fusion of portions of fetal anlagen. In other words, there were two distinct anlagen which would normally have progressed to the formation of twins if fusion had not occurred to produce hemihypertrophy.

In the case here reported there is a history of twins in the immediate family and of extensive cutaneous abnormalities of vascular origin. Whether one or both of these factors was directly concerned in the production of hemihypertrophy or whether some other influence was at work will, of course, remain a moot point.

The question as to why so many of these cases involve the right side is an interesting one. Embryologic studies fail to reveal any basis for such an occurrence. The circulatory system is slightly different on the two sides—the innominate artery arising from the arch of the aorta on the right to give off the right common carotid and right subclavian arteries, whereas on the left the common carotid and subclavian arteries branch directly from the arch of the aorta. This fact, however, offers no explanation as to why the right side should be more frequently involved in hemihypertrophy.

Finally, I should like to mention Milroy's disease, with which hemihypertrophy is occasionally confused. These two conditions are distinctly different. Milroy's disease is a hereditary disease in which edema of the lower extremities occurs in many members of the same family. In the early stages the edema is asymmetrical, affecting one leg before the other, but sooner or later both legs become involved. The edema and the hereditary phase definitely distinguish the disease from hemihypertrophy.

SUMMARY AND CONCLUSIONS

1. An unusual congenital, anatomic anomaly is presented.

2. No mental impairment accompanied the hemihypertrophy.

3. Nevi and telangiectases were scattered profusely throughout the surface of the skin.

4. Interrupted twinning, as propounded by Gesell, is the most likely etiologic factor.

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Progress in Pediatrics

CYSTS AND DIVERTICULA OF INTESTINAL ORIGIN

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Cysts and diverticula arising from the gastro-intestinal tract constitute a group of congenital malformations which not only present problems in clinical diagnosis but are of pathologic interest on account of their origin. The problem is still in a controversial state, particularly from the standpoint of the origin of certain of these anomalies.

The typical Meckel's diverticulum is single and arises from the antimesenteric border of the ileum. It may lie free in the peritoneal cavity, attached only at its point of origin from the bowel, or may exist as a patulous duct or a fibrous cord connecting the intestinal tract with the umbilicus or as a blind sac or cord attached to adjacent structures in the abdomen. Besides this classic type of fetal remnant of the vitelline duct, cysts of enterogenous origin have been described on the same embryologic basis. These may occur in the region of the umbilicus, in the abdomen independent of the mesentery or merely attached to it. Little has been added to the knowledge of the origin of this group of anomalies since Meckel's monograph.[1]

However, another type of the diverticulum and cyst of gastro-intestinal origin has been described, which, because of its position or its unusual relation to the gastro-intestinal tract, is separable from the type described by Meckel and subsequent writers on the subject.

From the standpoint of the origin of this group of anomalies the authors are divided into two schools, namely, those who consider all enterogenous cysts and diverticula as arising from remains of the vitelline duct, and those who consider the intramesenteric cysts and diverticula, duplications of the esophagus, mediastinal enterogenous cysts and duplications of the colon as having an independent mode of origin.

The following case brings up the controversial points involved and illustrates the usual clinical syndrome encountered.

From the Departments of Pediatrics and Pathology, College of Medicine, University of Illinois.

1. Meckel, J. F.: Handbuch der pathologische Anatomie, Leipzig, C. H. Reclam, 1812, vol. 1, p. 553.

REPORT OF A CASE

History.—R. S., a white boy, aged 29 months, was admitted to the hospital with the following history: At the age of 18 months the patient was seized for the first time with a sudden violent abdominal pain, crampy in character, which doubled him up. The attack was not associated with fever or gastro-intestinal symptoms. The duration of the attack was short, and the patient recovered without residual symptoms. His general health was good at the time, and the attack was attributed by the parents to teething. However, a week later the same set of symptoms was repeated, and during the following two months attacks recurred at intervals of one or more weeks. At 20 months of age, the patient became febrile, vomited and passed a considerable amount of bright red blood in the stool. While the amount of hemorrhage could not be estimated, the child was weak and drowsy after an attack. Four months later the abdomen was found to be enlarged, but no masses were palpable, and a routine roentgenogram of the chest disclosed a large area of increased density, extending from about the fourth dorsal vertebra to the diaphragm. This mass was globular in outline and displaced the heart to the left. In spite of the apparent size of the tumor, no respiratory symptoms were noted, nor could physical signs be elicited to indicate its presence. Deep roentgen therapy was without effect on the size of the tumor. During the nine months preceding admission to the Research Hospital, the attacks of abdominal pain recurred, often associated with the passage of dark red blood mixed with mucus by way of the rectum. Progressive weakness and anemia were present, apparently as the result of the repeated intestinal hemorrhage.

The birth, feeding and developmental history were normal. The patient had had bilateral otitis media at 9 months of age. The father had had syphilis before this infant was born, but was treated, and the Wassermann reaction was negative.

Physical Examination.—Though the child appeared weak and pale, he was fairly well nourished. Positive physical findings, except for a marked secondary anemia, were noted only in the chest and the abdomen.

The thorax was normal. On percussion, dulness was elicited posteriorly in the left intrascapular area, extending from the third to the fifth dorsal spine, and the breath sounds were decreased over this area. Tactile fremitus and vocal fremitus were normal. The apex beat was displaced to the left. Percussion dulness appeared to be increased to the left, and the heart sounds were poorly heard over this area.

The abdomen was slightly protuberant. The liver was palpable 3 cm. below the costal margin. No masses or tenderness was noted.

Roentgen examination (fig. 1) showed the following changes: Roentgenograms of the spine, made in the anteroposterior and lateral directions, showed an anomaly of development in the upper dorsal region and a localized area of increased density was seen to extend from the fourth dorsal vertebra to a point behind the diaphragm and laterally almost to the wall of the right side of the chest. The heart was displaced to the left. A lateral view showed the tumor to lie posteriorly in relation to the spine, and after the administration of barium the lower end of the esophagus was found displaced anteriorly. Marked gastric stasis was demonstrated in the roentgenograms taken following an opaque meal, without any apparent organic pathologic changes in the gastro-intestinal tract.

The urine was negative.

Examination of the blood showed: hemoglobin, 28 per cent (Sahli); red cells, 4,120,000, and white cells, 10,500. A differential count showed 62 per cent polymorphonuclears, 33 per cent lymphocytes, 4 per cent monocytes and 1 per cent basophils. No abnormal forms of leukocytes were noted.

Wassermann reactions of the spinal fluid and the blood were negative.
The stool contained occult blood and mucus.
Pirquet and Mantoux tests gave negative results.

Course.—While in the hospital, the patient had several severe attacks of acute abdominal pain, which he localized to the para-umbilical region. He was doubled up during these attacks but the pain apparently did not radiate. The attacks had no relation to the ingestion of food, and while vomiting and melena were frequently associated symptoms, they were not constant. The pain was often of such severity that narcotics were necessary for relief. Improvement in the patient's general condition followed two transfusions of blood, and the patient was discharged from the hospital with the diagnosis uncertain. During the following nine months there was no recurrence of symptoms.

Fig. 1.—Anteroposterior view of the chest, showing the mediastinal tumor on the right side displacing the heart to the left.

After one year, however, the patient was readmitted to the hospital with severe abdominal pain, vomiting and the passage of dark red blood and mucus in the stool. Except for an increased degree of anemia, no change from the previous findings could be elicited. It was decided to undertake an exploratory thoracotomy. The tumor was exposed and found to be bound down to the lateral aspect of the vertebral bodies by dense fibrous tissue, which was separated with difficulty. The child reacted poorly to the operative intervention, and after twenty-four hours died.

Pathologic Observations.—The tumor (fig. 2 *A*) removed surgically measured 12 by 10 cm.; it was slightly ovoid and fluctuant. The surface was smooth and pearly gray. The tumor was filled with grayish-yellow grumose material, which contained many cholesterol crystals. The capsule averaged 5 mm. in thickness, except at one area near the lower pole, where a sharply demarcated, projecting

mass averaging 8 mm. in thickness and 2 cm. in diameter was found. The lining surface was smooth and glistening and a pale gray.

Autopsy.—The well nourished and developed body displayed, in its pale waxy skin and pale and faintly cyanotic mucous membranes, evidence of marked enemia.

The site of the cyst removed at operation was marked by an area extending from the second to the seventh thoracic vertebra. The vertebral bodies in this region were asymmetric owing to moderate atrophy of their right halves, and they, as well as the first part of the corresponding ribs, were denuded of pleura. Below this area and separated from it by intact pleura, there lay cradled extra-

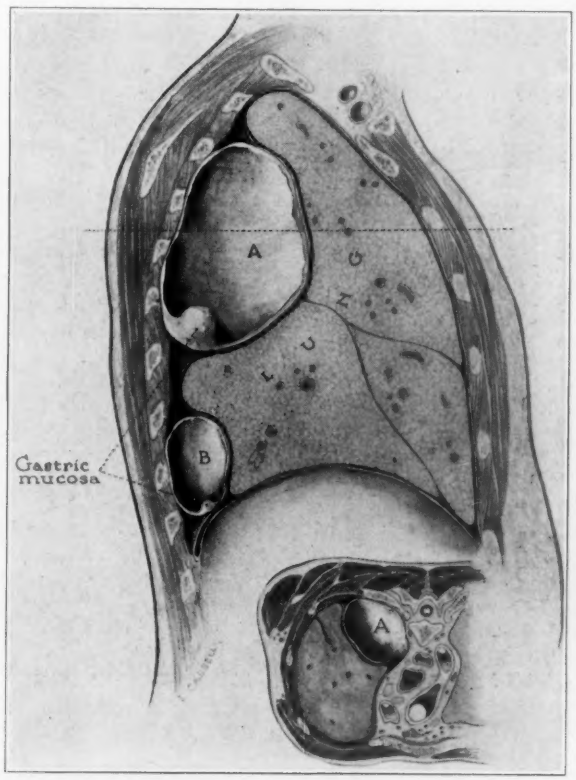

Fig. 2.—Semidiagrammatic sketch of the mediastinal enterogenous cysts. *A* indicates the cyst removed at operation; *B*, the cyst found at autopsy. The two are connected by rather indefinite fibrous strands. The dotted line indicates the plane of section diagramed below.

pleurally in the curve formed by the eighth and ninth vertebral bodies and the origin of the corresponding ribs, an egg-shaped, smooth, glistening, pale gray, fluctuant tumor measuring 6 by 3 cm. (fig. 2*B*). This cyst was filled with a pale, opalescent, straw-colored fluid in which floated many shining cholesterol crystals. Its lining was smooth and pearly gray, and the wall was 2 mm. in thickness, save in a sharply defined area 1.5 cm. in diameter, where it was thickened to 6 mm., and the lining was pale grayish pink and lusterless. At a point

20 cm. above the ileocecal valve, the ileum communicated through a 1 cm. sleeve-like opening with an aberrant loop of intestine 51 cm. long, running cephalad, parallel and in juxtaposition to the small intestine (fig. 3). It lay between the leaves of the mesentery and the mesenteric vessels. The latter divided, partially encircled the diverticulum furnishing its blood supply and extended onto the contiguous normal intestine. In its terminal 8 cm. only was the diverticulum separated from the normal bowel by mesentery. A second communication between the intestine and the diverticulum was found 12 cm. above the first. This opening was circular, measured 1 cm. in diameter and was the seat of a 1 by 10 mm. linear ulceration having a clean, grayish-red base and sharply defined edges. The lumen of the diverticulum, which was slightly smaller than the adjacent intestine, contained bloody mucoid material, and its identity was indicated by the plica cir-

Fig. 3.—Semidiagrammatic sketch of the intestinal diverticulum. The levels at which photomicrographs were made are indicated (*1, 2, 3* and *4*).

culares present throughout its length except in the terminal 5 cm. This latter region was the seat of a succulent, grayish-pink, velvety, mushroom-like excrescence 2 cm. in diameter and rising 1 cm. above the level of the surrounding mucosa. The excrescence was attached by a broad low pedunculated base. Beside the base and partially hidden by the overhanging tumor was a 1 mm. orifice opening into a 1.5 cm. cavity distended with thick dark brownish-red fluid. The walls of this cavity were smooth, glistening and mottled dark gray to dark red. From this cystic space a second 0.5 mm. opening into a second mucous membrane-lined cavity was found, and from the second cavity a gross constriction opened into a terminal mucus-filled pouch.

Except for a pronounced anemia of the parenchymatous organs, no further pathologic changes were noted.

Microscopic Appearance: A section of the diverticulum in area *1* of figure *3* (fig. 4) duplicated the microscopic picture of the proximal end of the jejunum. The plica circulares were prominent; the musculature was somewhat hypertrophic, and the myenteric plexus was clearly defined.

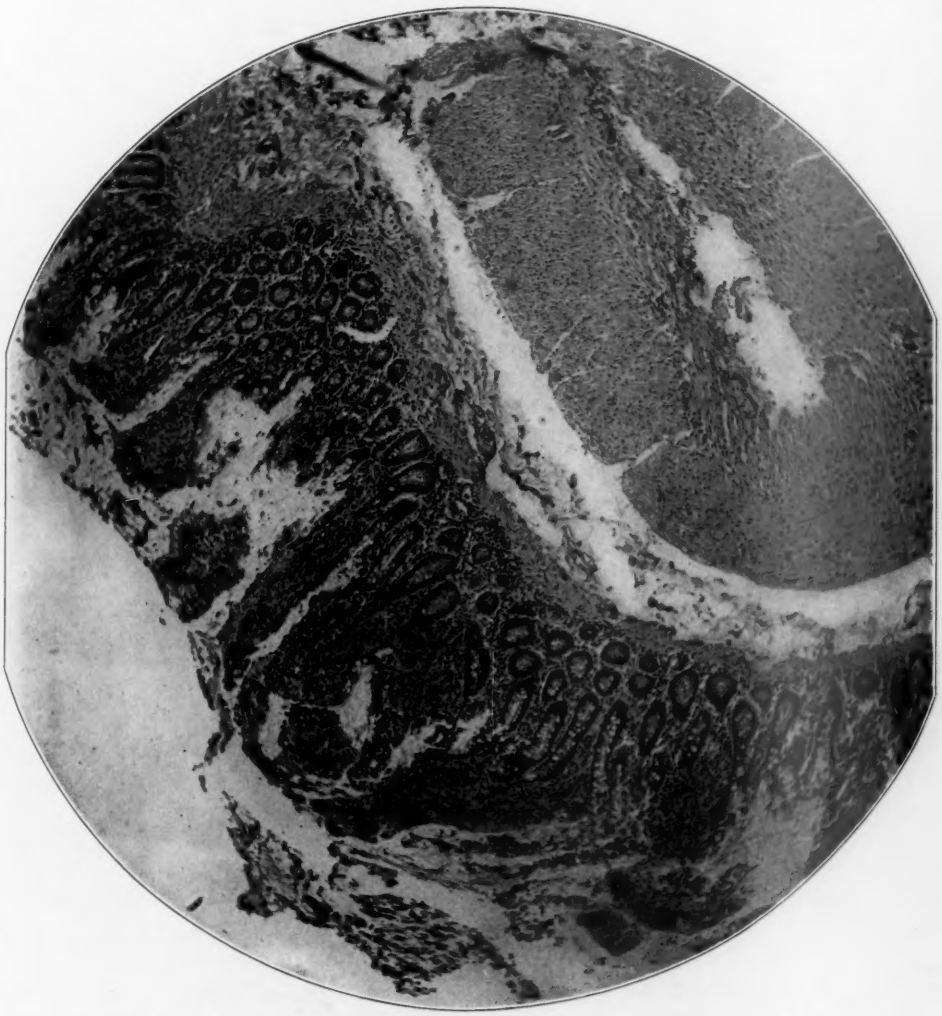

Fig. 4.—Section *1*, from the first part of the diverticulum (fig. *3*).

In sections from area *2* in figure *3*, a microscopic picture transitional between the small intestine and the stomach was found without clearly defined chief and parietal cells being present.

Sections from area *3* in figure 3 were readily recognizable as gastric mucosa with well defined chief and parietal cells. The muscularis was somewhat atypical in that it was made up of two well defined layers which were doubled over in one area to form a wall four layers thick.

Sections from area *4* in figure 3 (fig. 5) corresponded in detail to the section from area *3*, the mucosal layer, however, being thicker.

Sections from the wall of the cyst displayed three well defined muscular layers. The mucosa was replaced by old scar and granulation tissue, except at points indicated as gastric mucosa in figure 2. Here (fig. 6) the picture corresponded to that seen in area *3* of the diverticulum and was readily recognizable as gastric mucosa.

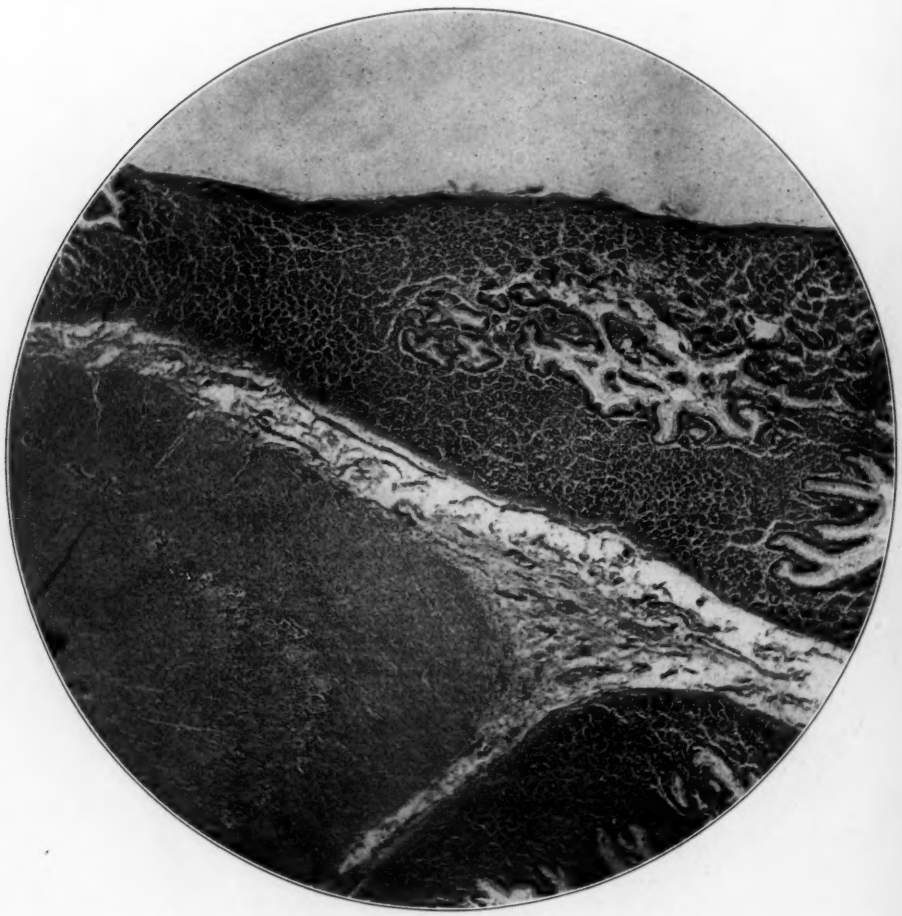

Fig. 5.—Section *4*, from the polypoid mass indicated in figure 3.

Résumé.—The anatomic findings included: (1) an intramesenteric diverticulum arising from the ileum and containing in its wall gastric mucosa and a polyp composed of gastric mucosa and terminally constricted to form incompletely separated cysts; (2) a peptic ulcer of the ileum at the upper point of communication with the diverticulum (probably the source of hemorrhage clinically); (3) extrapleural enterogenous cysts of the mediastinum made up of gastric mucosa, the largest part of

which had undergone pressure atrophy and perhaps digestive necrosis; (4) pressure atrophy of the bodies of the second to seventh ribs, inclusive, secondary to the presence of the large mediastinal cyst, and (5) atelectasis of the right lung and anemia of the parenchymatous organs.

REVIEW OF THE LITERATURE

This case presents certain clinical and pathologic features that are pertinent to the controversy on the origin of these anomalies. Students

Fig. 6.—Section from the persisting mass in the wall of the cyst, indicated in figure 2 as gastric mucosa.

of the subject vary widely in their opinions as to the origin of intramesenteric cysts and diverticula and mediastinal enterogenous cysts.

Roth [2] described a diverticulum of the ileum lying between the vessels of the mesentery and associated with an intramesenteric cyst and a mediastinal enterogenous cyst, and he referred to similar cases reported by Roesfeld [3] and by Hennig.[4] He considered the abdominal

2. Roth, M.: Virchows Arch. f. path. Anat. **86**:371, 1881.
3. Roesfeld, cited by Roth.[2]
4. Hennig, C.: Centralbl. f. Gynäk. **17**:398, 1880.

diverticulum and cysts as definitely derived from the vitelline duct, and concurred with Hennig in explaining the intramesenteric position of these structures by shortening of the mesentery of the diverticulum, thus drawing the appendage between the leaves of the dorsal mesentery. The mediastinal cysts were considered as originating by the pinching off of the embryonic esophageal diverticula or from the vitelline duct before development of the diaphragm. Since Roth's elaborate report but few similar cases have been recorded in the literature.

Fitz [5] described a similar intramesenteric diverticulum of the ileum as well as two instances of diverticulum lying on the antimesenteric border but having a common serous coat with the ileum. He concluded that "most if not all duplications of the intestinal tract in any part of its course originate from the vitelline duct, since that structure may vary widely in its relation to the intestinal segments and to the mesenteric attachments."

Buzzi [6] described a short intramesenteric diverticulum of the jejunum about 1 mm. below the ligament of Treitz.

Fröhlich [7] reported a case of diverticulum of the jejunum which was intramesenteric in position and lay in close contact with the bowel. He referred to it as a jejunum duplex.

Abt and Strauss [8] reported two cases of intramesenteric diverticulum of the ileum. They considered them as unusually located Meckel's diverticula, and emphasized the importance of intestinal hemorrhage in the symptomatology.

Struthers [9] reported two such cases. These authors ascribed the anomaly to vitelline duct rests and took issue with Miller,[10] who ascribed an intramesenteric cyst to sequestration from the bowel.

Barták and Diviš [11] reported a 58 cm. intramesenteric diverticulum of the ileum with the structure of small bowel, and ascribed it to sequestration from the intestine.

Tisdall [12] described an intramesenteric diverticulum of the ileum, and reported another case from the Hospital for Sick Children (Toronto) in which the proximal one third of the diverticulum lay between the leaves of the mesentery, and the distal two-thirds projected free of the mesentery. Without entering into a discussion of the possible

5. Fitz, R. H.: Am. J. M. Sc. **88:**30, 1884.

6. Buzzi, F.: Virchows Arch. f. path. Anat. **100:**357, 1885.

7. Fröhlich, A.: Ein Fall von Jejunum duplex, Inaug. Diss., Halle, 1891.

8. Abt, I. A., and Strauss, A. A.: Meckel's Diverticulum as a Cause of Intestinal Hemorrhage, J. A. M. A. **87:**991 (Sept. 25) 1926.

9. Struthers, J. S.: Edinburgh M. J. **37:**403, 1930.

10. Miller, R. T.: Bull. Johns Hopkins Hosp. **24:**316, 1913.

11. Barták, F., and Diviš, J.: Časop. lék. česk. **68:**1785, 1929.

12. Tisdall, F. F.: An Unusual Meckel's Diverticulum as a Cause of Intestinal Hemorrhage, Am. J. Dis. Child. **36:**1218 (Dec.) 1928.

embryologic origin, he considered these tumors examples of true Meckel's diverticula.

Borrman,[13] in his report of a similar completely intramesenteric diverticulum, was emphatic in deriving it from an unusually placed Meckel's diverticulum, and took issue with Fröhlich in describing his case as a duplication of the bowel.

Osler [14] described fifty-three diverticula varying in size from that of a cherry to that of a small apple and occurring on the antimesenteric border of the jejunum.

Moll [15] described a diverticulum arising from the antimesenteric border. Two ulcers were present in the contiguous intestine. Clinically, intestinal hemorrhage was a prominent feature.

Intramesenteric cysts have been described frequently. In association with enterogenous mediastinal cysts, such cysts lying within the mesentery of the small bowel have been described by Schmincke.[16]

Among the many authors reporting mesenteric enterogenous cysts are Miller,[10] van der Bogaert,[17] Osler,[14] Deaver [18] and Slesinger.[19] Hedinger,[20] who reported one case of intramesenteric cyst, considered its origin as by the pinching off of a diverticulum. Haggard [21] described a cyst lying between the muscular layers of the ileum. Most of these authors considered the possibility of sequestration from the small bowel as a mode of origin. Evans and Keith,[22] in a general analysis of enterogenous cysts and diverticula, reported an intramesenteric ileocecal cyst, and expressed a definite opinion in favor of the embryonic intestinal diverticula described by Lewis and Thyng [23] as a source of intramesenteric cysts and diverticula as well as enterogenous cysts occurring elsewhere.

Buschi [24] considered the nodules of Lewis and Thyng as the source of the not infrequent diverticula of the duodenum.

An analogous group of anomalies has been described in relation to the esophagus. Diverticula are, of course, not uncommon. However, duplication of the esophagus with the parallel segment opening into the main viscus both above and below, as described by Meckel,[1] is

13. Borrman, R.: Deutsche med. Wchnschr. **58**:43, 1932.
14. Osler, W.: Ann. Anat. & Surg. **4**:202, 1881.
15. Moll, H. H.: Brit. J. Surg. **14**:176, 1926.
16. Schmincke, A.: Virchows Arch. f. path. Anat. **227**:12, 1920.
17. van der Bogaert, cited by Miller.[10]
18. Deaver, H. C.: Ann. Surg. **49**:618, 1909.
19. Slesinger, E. G.: Brit. J. Surg. **16**:333, 1928.
20. Hedinger, E.: Virchows Arch. f. path. Anat. **167**:29, 1902.
21. Haggard, W. D.: S. Clin. North America **10**:713, 1930.
22. Evans, A., and Keith, A.: Brit. J. Surg. **17**:30, 1929.
23. Lewis, F. J., and Thyng, F. W.: Am. J. Anat. **7**:505, 1907-1908.
24. Buschi, G.: Virchows Arch. f. path. Anat. **206**:121, 1911.

extremely rare. Enterogenous cysts lying in relation to, but completely separated from, the esophagus are by no means common. They have been reported by Wyss,[25] Smith and Stone,[26] Mixter and Clifford[27] and Roth[2] in association with intramesenteric cysts and diverticula, and by Schmincke[16] in association with an intramesenteric cyst. Mixter and Clifford considered the possibility of the pinching off of outbuds from the foregut at the time of development of the lungs as the embryologic origin of the anomaly.

Grohé[28] described a case of complete duplication of the colon, extending from the cecum to an opening in the posterior foregut, lying in close proximity to the main bowel in its entire course and associated with a double uterus and double vagina. Grawitz[29] described a similar anomaly, which involved only the ascending colon and the opening above and below into the main intestine.

Jackson and Ewell[30] described an enterogenous cyst in the transverse mesocolon.

Histologically, the diverticula and cysts described are similar in structure. They display a hypertrophic smooth musculature in layers, such as are seen in the intestines. A well defined submucosa has been described in the majority of cases, and a myenteric plexus has been noted in a few instances. The mucosa, when intact, has been found to be identical with that met in the gastro-intestinal tract. In the cysts particularly, varying degrees of destruction of the mucosa by pressure, inflammation or perhaps digestive influences of the juices secreted have been described. Plica circulares are generally observed in the diverticula, but villi have been but rarely noted. Evans and Keith[22] stated that, because of the normal potentialities of the intestinal epithelium, epithelium and glands of any type occurring normally in the gastro-intestinal tract or its embryonic derivatives may be met with. The reports in the literature and our own case indicate that duplication of the small intestinal structure as well as the gastric mucosa is common.

COMMENT ON EMBRYOLOGIC ORIGIN

From the standpoint of the possible embryologic origin, it is difficult to correlate the wide variety of positions of these enterogenous diverticula and cysts, of which our case is an example, with vitelline duct rests. Lewis and Thyng[23] described knoblike groups of epithelial cells derived from the intestine and occurring along the course of the esopha-

25. Wyss, H.: Virchows Arch. f. path. Anat. **51**:143, 1870.
26. Smith, L. W., and Stone, J. S.: Ann. Surg. **79**:687, 1924.
27. Mixter, C. G., and Clifford, S. H.: Ann. Surg. **90**:714, 1929.
28. Grohé, B.: Deutsche Ztschr. f. Chir. **57**:445, 1900.
29. Grawitz: Virchows Arch. f. path. Anat. **68**:506, 1876.
30. Jackson, J. A., and Ewell, G. H.: Wisconsin M. J. **28**:118, 1929.

gus, stomach and small intestine in pig embryos of from 5.5 to 24 mm., in rabbit embryos of from 5 to 41.6 mm. and in human embryos of from 4 to 32 mm. These cell groups were either entirely separated from the intestinal tract or joined to it, with a hollow center continuous with the intestinal lumen to form a true diverticulum. Volker [31] encountered a single diverticulum of this type in a pig embryo, and explained it as an accessory pancreas. Bermer [32] also noted similar anomalies in human embryos, and though they were anomalous in time and position, he associated them with the pancreas. Lewis [33] described such an aberrant nodule of epithelium in the muscularis of the stomach of an embryo 19.3 mm. long, and he also considered it an accessory pancreas.

Thus, we find well substantiated the not uncommon occurrence in embryos of diverticula or accessory epithelial nodules which probably

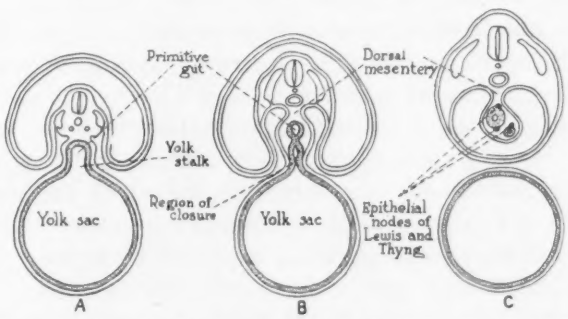

Fig. 7.—Cross-section of a 3 to 5 mm. embryo, indicating the methods of closure and the potentialities for sequestration. In *C*, the possible locations for the epithelial nodes of Lewis and Thyng are indicated. (After Kampmeier.)

ordinarily disappear. Theoretically, these aberrant nodules may originate in either of two manners: First (fig. 7), they may arise as sequestrations in the process of development of the anterior abdominal wall, narrowing and finally pinching off the vitelline sac, i. e., in the separation of the fore and hind intestine from the yolk sac, as suggested by Kampmeier.[34] Second, they can be accounted for as supernumerary outgrowths, the prototypes of which give rise to the lungs, pancreas and liver. In certain of the lower fishes multiple diverticula occur in the region of the duodenum, a fact recorded by Schminkewitsch.[35] While these structures serve no apparent function, they offer a partial

31. Volker, O.: Arch. f. mikr. Anat. **59**:62, 1902.
32. Bermer, J. L.: Am. J. Anat. **5**:474, 1906.
33. Lewis, F. J.: Am. J. Anat. **13**:477, 1912.
34. Kampmeier, O.: Personal communication to the authors.
35. Schminkewitsch, W.: Lehrbuch der vergleichenden Anatomie der Wirbeltiere, Stuttgart, E. Schweizbart'sche Verlagsbuchhandlung, 1910, p. 431.

phylogenetic explanation of the nodes of Lewis and Thyng. Regardless of their mode of origin, however, they occur in positions and at a time when their persistence and subsequent development would place them between the leaves of the mesentery or in the thoracic cavity.

It may further be pointed out that at the time of obliteration of the vitelline duct in the 7 mm. embryo the dorsal mesentery and its vessels are already well developed. In the case of the intramesenteric cysts and diverticula it is necessary to postulate that the duct remnants not only insert themselves between the well formed leaves of the dorsal mesentery, but also between its vessels, deriving an entirely new blood supply from them. It therefore appears more logical to consider the epithelial nodes of Lewis and Thyng as the source of those rare enterogenous cysts and diverticula lying within the mesentery, as well as those found in a position far removed from the site of the vitelline duct, i. e., in the thorax.

Since the developmental potentialities of the gastro-intestinal mucosa are wide, the histologic structure of the fully developed anomaly is of no aid in determining its origin.

The rare instances of duplication of the colon, such as that described by Grohé [28] and by Grawitz,[29] certainly require an explanation other than persistence of remnants of the vitelline duct. Simple duplication, perhaps by the formation of an anomalous septum, appears to be the simplest explanation, although again the epithelial nodes of Lewis and Thyng [23] must be considered as a source of origin.

On the basis of these points, as well as the not infrequent association of mediastinal enterogenous cysts with the intramesenteric cysts and diverticula (a combination as yet unreported with a typical Meckel's diverticulum), this group of anomalies should be separated on the basis of their embryologic origin from the true vitelline duct rests. The epithelial nodules of Lewis and Thyng [23] are their probable source, although one cannot rule out entirely simple duplication of intestinal segments.

CLINICAL FEATURES

Such controversy as may exist with regard to the embryologic origin of the various types of enterogenous cysts and diverticula is of no great clinical importance. On the other hand, the difficulties in diagnosis offered in general by enterogenous cysts and diverticula, whether of the typical Meckel's or the intramesenteric type, are of the greatest practical significance.

Enterogenous cysts in the mediastinum differ in no wise in their symptomatology from the benign tumors occurring in this region. They cause symptoms purely as a result of pressure, although gradual growth may allow large size without the manifestation of any clinical evidence

of their presence. Because of their position in relation to the esophagus and behind the pleura, they tend to project into the corresponding pleural cavity (usually the right), compressing the lung and secondarily displacing the heart. As in the case here described, the pressure on the vertebral bodies may be sufficient to cause atrophy and deviation of the bony structures, a deformity that was erroneously considered congenital by Schmincke.[16]

The enterogenous cysts occurring in the abdomen similarly may cause symptoms by pressure on contiguous structures. Colicky pain is not an infrequent symptom, which, in view of the structure of the tumor, might be explained on the basis of contractions of its muscular wall, and not directly as the result of increased pressure within the cyst. This conclusion is drawn from the fact that the growth of these cysts and the secretion of material into them are usually slow and not likely to cause acute attacks of pain. The cysts may reach sufficient size to be palpable clinically as a more or less movable abdominal mass.

The direct symptoms noted with diverticula, both of the typical Meckel's variety and more commonly with the intramesenteric type, are chiefly colicky pain and intestinal hemorrhage. The first symptom is probably due to the strong contractions undergone by the musculature in the walls of the tumor, which reach the level of pain when the diverticulum contains accumulated secretions, resulting in an increased strength of the contractions. In many cases the hemorrhage is accounted for by ulcerations in the intestine at or near the opening into the diverticulum or in the intestinal mucosa of the diverticulum. The not uncommon presence of gastric mucosa in the diverticulum suggests the possibility that the secretion of such heterotopic rests may stand in causal relation to the ulceration. Occasionally, such ulcerations may perforate, as in the case reported by Singer and Vaughan.[36] These authors were able to collect fourteen cases of perforated peptic ulcer of the diverticulum. In all but five, histologic demonstration of a digestive ulcer was possible. In contrast to their rare occurrence in intramesenteric diverticula pathologic changes, such as acute inflammation (diverticulitis), torsion and intussusception causing clinically intestinal obstruction, are not uncommon in the typical Meckel's diverticulum. This frequency is explained by the mobility of this latter type of diverticulum. Thus, Porter,[37] in an analysis of one hundred and eighty-four cases of abdominal crisis caused by Meckel's diverticula, listed intestinal obstruction, intussusception and diverticulitis as the etiologic factors.

36. Singer, H. A., and Vaughan, R. T.: Ann. Surg. **96**:230, 1932.

37. Porter, M. F.: Abdominal Crises Caused by Meckel's Diverticulum, J. A. M. A. **45**:883 (Sept. 23) 1905.

From the cases reported, the association of a symptom complex occurring with Meckel's diverticula, intramesenteric diverticula and enterogenous cysts has occurred most commonly in male patients. The symptoms have usually been noted first during infancy or childhood. Intestinal hemorrhage, while a frequent symptom, has varied in both frequency and amount. In some cases there is only a single hemorrhage followed by a period of apparent recovery for months or years. In one case reported there was a profuse hemorrhage during infancy and no further symptoms until the age of 18, when the patient died as a result of marked intestinal bleeding or shock. In other cases melena occurred at more or less frequent intervals. Abdominal pain is likewise variable in intensity and location. In many cases the pain was indefinite and difficult to localize, while in others the symptom was of severe colicky nature and referred to the right upper quadrant or the para-umbilical region. While the association of these symptoms in the absence of a specific cause should suggest the presence of an anomaly of this type, the symptoms are closely simulated by intussusception, and few cases have been correctly diagnosed before operation or postmortem examination. Little aid has been afforded by the x-rays or other methods of examination. Fever is notably late in its inception or entirely absent except in the rare instances of primary diverticulitis encountered in cases of true Meckel's diverticula.

In our case the obscure abdominal pain and intestinal bleeding gave a picture that was complicated by the presence of a large mediastinal tumor. However, in view of the frequent occurrence of mediastinal enterogenous cysts and abdominal enterogenous cysts and diverticula together, as reported in the literature, the combination, while rare, when met with is characteristic.

SUMMARY

1. A case of enterogenous cysts of the mediastinum containing gastric mucosa and an intramesenteric cyst of the ileum containing gastric mucosa is reported.

2. Attention is redirected to the epithelial nodes and diverticula reported by Lewis and Thyng [23] as a probable source of origin for these rare anomalies.

3. A common clinical picture, such as occurs in cases of intestinal diverticula is drawn, and emphasis is again placed on the occurrence of obscure abdominal colic and unexplained intestinal hemorrhage.

STAMMERING AND STUTTERING, THE PEDIATRICIAN'S RESPONSIBILITY

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The indifferent attitude manifested by the medical profession toward the subject of speech disorders is nothing short of lethargy. Proof of this statement can be obtained from the declarations of parents who quote the doctor as having said that the child will outgrow the speech defects.

Although incorrect speech is less frequent after adolescence, it is not because the children necessarily "outgrow" their affliction. By the increased powers of observation and imitation and by the constant association with normally speaking people, many children of themselves learn to speak correctly. If all children would behave in this way there would never occur any speech disorders in adults. However, as long as there are people who go through life with speech defects, the problem exists.

Before the lay public can appreciate the fact that some good can be done, the physicians themselves must learn more about how to handle these cases. It is not the purpose of this paper to expound any new theories but merely to awaken interest in something which should be more generally appreciated. Regardless of the type of disorder, there should be two avenues of approach, namely, the psychologic and the mechanical. Psychiatrists and psychologists are apt to emphasize the former and elocutionists and teachers the latter. Both methods are important and should be employed concurrently in order to get a satisfactory result. The pediatrician is ideally equipped to handle the problem from both points of view provided that he acquaints himself more thoroughly with the methods at hand.

Parents are prone to disregard speech disorders during childhood because they consider them a process of normal development and are even apt to regard them as "cute." The same conditions, however, if prolonged into adult life may lead to serious consequences. A marked speech disturbance is nearly always accompanied by decided feelings of inferiority and may oftentimes even lead to an unsocial existence. For this reason early treatment is imperative. However, parents do not realize this. In spite of the fact that the speech disorder may be

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marked, it is, indeed, rare for the parent to consult the physician for its correction. It is usually the doctor who brings the mother's attention to the imperfection. When the physician manifests an interest and sounds the proper warning, the parents are generally anxious to cooperate in eradicating the difficulty.

The rôle of conditioned reflexes is all-important. If a child is in the habit of obtaining candy when it asks for "tandy," there is little need for further effort because the desired result is obtained. Repetition of this performance tightens the bond of the sensory-motor pathways so that the letter "k" will be pronounced like the letter "t." Such a bond once formed is usually broken with great difficulty. Parents must be taught how to "recondition" the child in the other direction. In many instances the child had been able to make the correct sounds but does not do so because of failure to train the proper associations.

I shall eliminate from this discussion the speech disorders based on organic pathologic conditions such as harelip, cleft palate, tonguetie and the like.

Some speech disorders are based on nervous disturbances far below the psychic level. Among these are the cases that are attributed to the change of handedness. There are some investigators who claim that they have accomplished excellent results on having such patients return to the original handed state. My experience has failed to discover a case to fit into this category. It is, however, worthy of investigation. Other speech defects based on disorders of the nervous system as in chorea will coincide in their course with the existing nervous disease.

DIAGNOSIS AND TREATMENT

In this country it is customary to interchange the terms "stuttering" and "stammering." If the words are not considered synonymous, the fine distinction consists of applying the term stammering to the involuntary breaks or stops in utterance and stuttering to the hesitancy before the words are uttered, or vice versa. In Europe, however, stuttering is taken to include the two foregoing conditions and stammering is employed to mean the inability to articulate consonants correctly. Lisping and kindred disorders are, therefore, included in the latter category.

Stammering (in the European sense) can be of two types: universal and partial. In universal stammering many sounds are disturbed so that an entirely different word form may be produced. A few examples should illustrate what is meant. The child may say "twipt" in attempting to say "swift" or "zit" for "this" or "titten" for "chicken."

Universal stammering occurs in self-centered children. Their speech is essentially primitive, as in a baby learning to talk or as in savage

peoples. The ordinary child learns that it is necessary to speak like its parents. These children endeavor to have others learn their language.

In this type as well as in partial stammering the correct speech melody is maintained, although the articulation is poor. In attempting to treat universal stammering, it is necessary to separate the defects into their component parts. As partial stammering involves difficulty in one or two sounds, universal stammering includes many mispronounced consonants.

The main defects are classified according to the letters mispronounced, as follows:

I. Sigmatismus
   (*a*) Interdentalis
   (*b*) Lateralis
   (*c*) Addentalis
   (*d*) Nasalis
II. Rhotacismus
III. Kappacismus

Sigmatism means the incorrect articulation of the sound "s". The correct way of making this sound is to raise the lateral parts of the tongue so that a central gutter is formed on the dorsum along which the air is blown. The tip of the tongue is at the floor of the mouth. If voice is used when this sound is made, the sound of the letter "z" is produced.

If the sigmatism involves the placing of the tongue between the teeth, the condition is known as sigmatismus interdentalis. Many patients showing this disturbance will also mispronounce the second sound with the tongue between the teeth, so that the letters "t," "d," "n" and "l" will not be spoken correctly. This is termed multiple interdentalism.

If both lateral portions of the tongue are not elevated uniformly, so that the air is blown to one side, the condition known as sigmatismus lateralis is produced.

Some patients are able to hold the tongue in the proper position, but by not holding the soft palate in contact with the posterior wall of the pharynx, blow the air through the nose. This is known as sigmatismus nasalis.

The term sigmatismus addentalis is applied to the pathologic state in which the tip of the tongue approximates the upper teeth so that there is insufficient space for the air to pass through. The extreme degree of this disorder is that in which the sound "t" is said instead of "s." It is a rather rare condition. The presence of this disorder is almost always a symptom of congenital disease of the internal ear or an otitis during the first year of life. The hearing apparatus having been so involved, the hissing sound of the letter "s" is not perceived correctly,

hence it cannot be imitated properly. The patients rarely are aware that they have a speech disorder in this condition as they have no acoustic control.

The prognosis for sigmatism is good except for the addental type, which can sometimes be helped but for which no guarantees can be given. From one to two months is required to bring about a cure, during which time the child should be seen from three to four times a week.

The child should be treated alone and handled with utmost pedagogic tact. During the early stages the patient is not to know what is aimed at by the treatment. The parents are not to join in the management of the case.

Opportunity must be given the child for observing the correct movements of the tongue and lips and watching his own movements in a small mirror. The child is asked to show the teeth and blow. If the sound is not produced correctly, a hollow key or vial is held firmly against the lower lip in such a way that when the air rushes over the opening a whistling sound is produced. When the key whistles, the "s" is being pronounced correctly. If the key is necessary in order to have the child blow the air properly, let him perform this way for a few lessons, then have him repeat the procedure without the key. Occasionally it is necessary to fashion a hard rubber device to fit on the patient's tongue so that the air can be blown in the proper manner.

After the letter "s" has been pronounced correctly for several lessons, the next step is to apply the sound to syllables. The exercise is to tell the patient to blow the air and then say "ha." The next time teach the child to make the same sounds with one expiration. The following visit tell the child not to emphasize the "h" so much. The child will soon be saying "sah" with greatest ease. The other vowels will follow in the same way, so that by this time the child can say, "so," "say," "see" and "sue."

The next step is to have the patient exercise two syllables that need not have any sense, as "so-sa," "soo-si" and "see-saw." After that, select words that have the sound "s" and have the child utilize the sound that was learned. If the child is able to read, the final step is to underline the "s" sounds on a printed page and practice the correct articulation by reading aloud.

The sound of the letter "z" is easily produced by having the patient vocalize or sing while pronouncing "s."

Kappacismus means the inability to pronounce "k" and hard "g." The latter is the same as the former but with added voice. It is an explosive sound formed by the posterior part of the tongue and the palate. The mistake made generally is to pronounce the sound "t" instead of "k."

By introducing a tongue depressor into the child's mouth and having him say "ta," the correct "k" will be produced. Have the mother or nurse exercise the child this way at home. At the next lesson the patient will understand what is expected and will produce the correct "k." Then train with syllables as in sigmatism. When the child articulates "k" well, he is apt to confuse "t" and "k," using them interchangeably. It is necessary then to exercise with a hand-raising movement the difference between "t" and "k" words.

In order to produce the hard "g" sound, exercise the sound "d" with a tongue depressor.

The letter "r" in the English language is treated very simply. By holding the tip of the tongue close to the hard palate a short distance behind the upper teeth and vocalizing, the correct sound is produced. The correct position may be difficult to find at first, but as soon as it is it should be encouraged and exercised.

The European rolled "r,'" however, is a difficult sound. It is treated by having the patient say "di-da" repeatedly until it sounds like "dr-r-ra." After obtaining this sound, the patient is asked to place a vowel before it to make "ad-dr-r-ra." From then on it is a comparatively simple matter to practice the rolled "r."

Stuttering is on the whole more difficult to treat than stammering. In this condition the patient is able to articulate the sounds properly but is hindered from doing so by a maze of psychic impediments. From the mechanical point of view the main difficulty lies in the inability to give proper volume to the vowel sounds. This, in turn, is due to disturbances in the respiratory mechanism. A stutterer will often show jerky respiratory movements instead of the normal short inspiration and long expiration.

The type of stuttering will vary with the length of time the child has been suffering from the disturbance. The simple repetition of syllables is considered the mildest form of the disorder and is termed clonus. The forced articulation is termed tonus. It is found together with clonus in stutterers who have been afflicted for a period varying from several months to a few years. A quick convulsive twitching of the muscles of speech, known as quick tonoclonus occurs somewhat later. The next stage shows a slow tonoclonus, helping purposeless movements of the face or body and the condition known as embololalia, which is the interpolation of meaningless words into the speech. The final stage is known as the *forme cache*, in which the patient tries to hide the condition by maintaining silence or speaking rather foolishly. This is considered by most investigators as the severest stage of stuttering.

Stuttering presents a vicious mental cycle. There are always strong psychic factors which start the child on a stuttering career, and there

are other forces which perpetuate and aggravate the condition. A violent mental shock or a slowly developing mental conflict will serve as etiologic factors in most cases. It is obvious that before one can hope to attain any measure of success, one must first investigate the child's past and present environment.

From the point of view of the pediatrician, the answers to tactful questioning of the parents and child will reveal some startling information. It is inadvisable to attempt to employ psychoanalysis. The use of this method on children is a comparatively new field of medical endeavor. Although it may be of great value in ferreting out obscure psychic disturbances, such drastic measures are generally not necessary in determining what is wrong. There are some, too, who believe that a great deal of harm can be done because during some phase of the analysis the child's adjustment to his environment is broken. Whatever there may be of value in the psychoanalytic approach both in the diagnosis and treatment, it is inadvisable for pediatricians to use these methods. They should be avoided not only on account of the dangers involved, but particularly because few pediatricians know how to employ psychoanalysis properly or interpret the findings.

In handling the minor psychologic aspects of the speech problem, the cure is easily effected as soon as the diagnosis is made. There are, however, cases which require more severe measures. It is necessary, in some instances, to hire a special nurse or teacher so that the parental contact may be temporarily severed. It is necessary to do this in cases in which the children are obviously neglected, as they are by some of the modern bridge-playing mothers, or excessively pampered, as is an only child of nervous parents or a child brought up by a grandmother.

When a child shows the earliest form of stuttering, the clonic symptom, it is best merely to adjust the psychic state without mentioning the speech disturbance. If too much attention is directed to the stuttering, the child attempts to correct it by speaking forcibly. In this way the tonic stage is arrived at.

The more severe forms of stuttering manifest neuroses secondary to the speech disturbances. In its extremest form, the patient exhibits an extreme dislike or morbid fear of speaking producing the state of mind known as lalophobia. Reassurance along these lines is, therefore, indicated.

Psychic treatment by suggestion in any form, although of extreme value, must also be accompanied by training. When the feeling of inferiority has been attacked so that the patient is at ease, the exercises will be more effective.

It is first necessary to teach the child how to breathe properly, in the beginning by the use of accessory muscles, as raising and lowering

the arms and later by controlling the muscles of the chest and abdomen. When the expiration is good, training of the voice is then started. This is done by having the forced expiration of the sound "h" followed by a vowel sound. This having been accomplished, have the patient break up the expiration by producing the sounds "ha-ha-ha" in rapid succession. A sharp jerky downward movement of the arms will help bring this about. The next effort is to produce the same tone effects with a minimum of air.

After this is attained the training of consonants follows. It may be necessary to demonstrate the correct position of the lips, teeth, tongue, etc., as in stammering. Then have the patient sing with different letters.

The keynote to the whole treatment is proper encouragement. Best results are obtained in private patients because of an interesting bit of practical psychology: If a flat fee is arranged for and paid in advance, the parents of the child will be far more cooperative in the treatment.

REPORT OF CASES

CASE 1.—C. S., a girl, aged 6 years, was brought in on Sept. 7, 1931, for the treatment of seasonal hay fever. The child exhibited universal stammering to such an extent that she was at times unintelligible.

It was noticed in the course of the examination that the child's attention wandered about the room. She picked up papers and instruments and asked a myriad of questions. Her personality was obviously of the egocentric type.

On analyzing the speech disturbance, it was found that the main components of her difficulty were extreme sigmatism addentalis and rhotacism. A course of treatment was undertaken without promising too much.

After two months of training by the use of a small vial to learn the correct "s" and constant drilling of syllables and words, she pronounced the "s" sound perfectly. The same applied to the letter "r." She spoke very clearly in the office where she knew that any mistake would produce an unfavorable reaction. However, at home she lapsed frequently into her former method of speech.

As she was an only child, it was found that at home she was treated like a much younger child. As a result, baby methods were encouraged. When the condition was explained, these lapses occurred less frequently. Her speech will, no doubt, be even better after she learns to read and forms the proper visual associations.

CASE 2.—B. J. G., a girl, aged 3 years, was brought to the office on March 7, 1931, for the treatment of an eczematous condition behind the ears and chronic blepharitis. No mention was made of speech disorders. However, in the course of examination it was revealed that the child exhibited hesitating, broken speech. A diagnosis of clonic stuttering of recent origin was made.

Investigation into the home surroundings of the child revealed that the mother was a school teacher in a nearby city. It was her custom to sneak out every morning without any knowledge on the part of the child and to return in the evening. The child was very much attached to her mother but was daily left in the charge of a housekeeper. When the child awoke she would invariably look for her mother.

After the condition was explained, a plan was formulated whereby the mother was to make a formal exit every morning in full view of the child. A few days of this regimen resulted in complete clearing of the speech disorder.

CASE 3.—S. K., a boy, aged 4, was brought into the office on June 22, 1931, for acute coryza and a general physical examination. He had been recently adopted from a public institution.

The history elicited a multiplicity of behavior disturbances including night cries and stuttering. The officials at the institution had not mentioned anything of this character before adoption. The foster mother was of the opinion that the child did not like his new surroundings.

When adequate investigation was made, it was determined that the child had been previously transferred several times. He was now in a situation best to his liking, but developed the peculiar behavior pattern as a result of fear that he might be taken away from home and thrust back into the institution.

After the child was convinced that now he was in his permanent home and would continue to have his mother's love and his pretty toys, the night cries and stuttering cleared completely.

CASE 4.—R. F., a girl, aged 7 years, was brought to the office on April 2, 1932, for an examination of the heart. On eliciting the history, it was disclosed that recently the child refused to allow her windows to be opened at night and began to speak peculiarly. The diagnosis was chronic rheumatic mitral disease and behavior disturbances.

Investigation into the home surroundings of the child revealed that she had been scared recently by stories of the kidnapping of the Lindbergh baby. She was in mortal fear of being kidnapped. When the child was reassured as to the improbability of such an occurrence, a complete mental readjustment was made. All nervous symptoms promptly cleared.

CONCLUSION

An attempt was made to elucidate some of the principles of handling cases of stammering and stuttering. It is the pediatrician's responsibility to recognize these conditions and to treat the patients.

15 West Lena Avenue.

Pediatric Biographies

JOHN FREKE
1688-1756

JOHN RUHRÄH, M.D.
BALTIMORE

John Freke, son of a surgeon of the same name, was born in London in 1688. He was apprenticed to Mr. Blundell, whose daughter he married. In 1726, he was made assistant-surgeon to St. Bartholomew's Hospital, and the same year was made curator of the museum when it was started. This museum was in a single room under the "cutting ward," and among other things it contained the stones which surgeons had removed, which previously had been placed in the counting room when patients paid their bills. In 1727, he was put in charge of the blind patients, and the governors passed a resolution:

> Through a tender regard for the deplorable state of blind people, the Governors think it proper to appoint Mr. John Freke, one of the assistant surgeons of this House, to couch and take care of the diseases of the eyes of such poor persons as shall be thought by him fit for the operation, and no other reward than the six shillings and eight pence for each person so couched, as is paid on other operations.

Times have changed! In those days a surgical operation was looked on as a glorified haircut, and the fee was charged accordingly.

In 1729, he was elected a fellow of the Royal Society. He was dexterous with his hands, and besides practicing surgery did wood carving as a diversion. He performed experiments in electricity and wrote a book about the subject, which contains many of his ideas; they are more interesting on account of their originality than for their accuracy. His interest in electricity led Fielding to mention him in "Tom Jones," and in the fourth book, where the contagiousness of Black George's switch is described, he says, "to say the truth, as they both operate by friction, it may be doubted whether there is not something analogous between them of which Mr. Freke would do well to enquire before he publishes the next edition of his book." The other reference is, "We wish Mr. John Fr—— or some other such philosopher would bestir himself a little in order to find out the real cause of this sudden transition from good to bad fortune."

It is recorded that he asked permission to bury his wife in St. Bartholomew's the-Less, or as the record has it: "allowed to bury her in the Poor's Chapple, he making good all damage and paying only single fees."

In 1755, when he resigned from the hospital, he made formal application to be buried beside his wife. There is no record of what was

done with the request, but when he died on Nov. 7, 1756, he was buried as he had wished. There is a bust of him in the hospital library.

He wrote "An Essay on the Art of Healing," which was published in London in 1748. He knew the difficulty of removing all the lymphatics in operating for cancer and what happened if any were left. He did early paracentesis in empyema, using a cannula for a drain.

Freke was fond of art and music and had many friends among both artists and musicians. In a life of Hogarth there is the story of how when Cheselden was dining with Hogarth he told how Freke a few nights before, at Dick's Coffee House, had said that Greene, the organist of St. Paul's, was as good a composer as Handel.

" 'That fellow Freke,' said Hogarth, 'is always shooting his bolt absurdly one way or another: Handel is a giant in music.' 'Ay,' said the informant, 'but at the same time Mr. Freke declared you were as good a portrait painter as Van Dyck.' 'There he was in the right,' added Hogarth, 'and so I am, give me my time and let me choose my own subject.' "

Michael Underwood, as a medical student, came in contact with Freke, who may be admitted to the ranks of pediatricians, as he was doubtless the first to describe myositis ossificans progressiva.

This is in the *Philosophical Transactions of the Royal Society of London,* 1736:

XXIV. A Letter from Mr. John Freke, F.R.S., *Surgeon to* St. Bartholomew's Hospital *to the* ROYAL SOCIETY, *relating a Case of extraordinary* Exostoses *on the Back of a Boy.*
Gentlemen:

I would not have troubled you with this Account of a Case which came to my Inspection Yesterday at *St. Bartholomew's Hospital,* had I ever seen the same before in my Practice. I know it may be said to come under the Denomination of an *Exostosis,* but as all others that I have seen, which have been very many, arose upon some particular Parts, and have not been found to proceed from a general Dissolution of the Bones, as this hath, I think fit to submit it to your Consideration. The Case is as follows: Yesterday there came a Boy of a healthy Look, and about Fourteen Years old, to ask of us at the Hospital, what should be done to cure him of many large Swellings on his Back, which began about Three Years since, and have continued to grow as large on many Parts as a Peny-loaf, particularly on the Left Side: They arise from all the *Vertebrae* of the Neck, and reach down to the *Os Sacrum;* they likewise arise from every Rib of his Body, and joining together in all Parts of his Back, as the Ramifications of Coral do, they make, as it were, a fixed bony Pair of Bodice. If this be found worthy your Thoughts, it will afford a Pleasure to,

GENTLEMEN,

Salisbury-Court, *Your most humble Servant,*
April 15, 1736. John Freke.

It is to be observed, that he had no other Symptom of the Rickets on any Joint of his Limbs.

Pediatrics in Art

TESTING TEMPERATURE

JOHN RUHRÄH, M.D.
BALTIMORE

The lying-in chamber was a favorite subject of artists, and many scenes were depicted. Many of these pictures have been collected in a volume by Dr. Robert Müllerheim, of Berlin, entitled "Die Wochenstube in der Kunst." A considerable number of them have pediatric

The Virgin and the Christ Child.

interests as well, such as the illustration of a Tyrol lying-in scene by an unknown master of the south Tyrol school. This shows the Holy Family. The head of the bed is protected from draughts and cold. The Child is about to be bathed, and in the absence of the present-day bath thermometer the nurse is using the homely but effective method of testing the water with her bare feet, showing a shocking lack of the precautions against infections now in vogue. Felix Würtz said about this: "Touching Baths of Children, it is known that they are bathed sometimes so hot, that the heat thereof is scarcely sufferable to an old bodies hand. . . ." He advised trying the water.

This painting is in Innsbruck.

News and Comment

GENERAL

Babies' and Children's and Maternity Hospitals, Cleveland, Closed.—The Babies', and Children's Hospital and the Maternity Hospital, members of the University Hospitals of Cleveland, have been temporarily closed because of scarcity of funds resulting from general and local financial conditions. Their activities will be carried on, on a reduced basis, in the new Lakeside Hospital and Hanna House buildings, the other members of the University Hospitals group, in which the departments of medicine and of surgery have made room to accommodate pediatrics and obstetrics.

Course on Child Development, University of Iowa.—At the University of Iowa a course from July 9 to August 24 on "Child Development and Parent Education," will be given by the instructional staff of the Iowa Child Welfare Research Station.

SOCIETY NEWS

Fourteenth International Congress of Radiology.—The congress will be held at Zurich, Switzerland, under the presidency of Prof. H. R. Schinz from July 24 to 31, 1934.

American Pediatric Society.—At a meeting of the society at Washington, D. C., on May 8, 9 and 10, Prof. E. Gorter of Leyden, Netherlands, was elected to honorary membership. The following were elected to active membership: Dr. Normal C. Wetzel, Cleveland; Dr. Alfred H. Washburn, Denver; Dr. Martha M. Eliot, New Haven, Conn.; Dr. George M. Guest, Cincinnati, and Dr. Russel Rowland, Detroit. The following officers were elected: president, Dr. Charles A. Fife, Philadelphia; vice-president, Dr. Samuel W. Clausen, Rochester, N. Y.; secretary-treasurer Dr. Hugh McCulloch, St. Louis; recorder and editor, Dr. C. A. Aldrich, Winnetka, Ill., and member of the council, Dr. S. G. Ross, Montreal, Canada. The next meeting will be held at the Grove Park Inn, Asheville, N. C., early in May, 1934.

UNIVERSITY NEWS

Dr. J. C. Gittings of Harwood, Md., one of the members of the editorial board of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, has accepted the William H. Bennett professorship of pediatrics, School of Medicine, University of Pennsylvania.

DEATHS

Dr. J. Hutinel, a well known pediatrician of Paris, and son of the eminent French pediatrician, Dr. Victor Hutinel, died recently after a short illness.

Obituary

THOMPSON SEISER WESTCOTT, M.D.
1862–1933

Dr. Thompson S. Westcott was born in Philadelphia on June 11, 1862. He was a son of Thompson Westcott—lawyer, journalist and historian. In his boyhood Dr. Westcott attended the Friends School, and later entered the college department of the University of Pennsylvania, graduating in 1882 with the degree of B.A. While in college, he edited the *University Magazine* and *Class Record*. After graduating, he taught Latin and Greek in Rugby Academy.

Dr. Westcott entered the medical department of the University of Pennsylvania in October, 1883, graduating with the degree M.D. in 1886.

He served as intern at the University Hospital from 1886 to 1888, and at the Pennsylvania Hospital during 1888 and 1889. He practiced his profession in Philadelphia from 1889 without interruption until his death, which occurred on Jan. 28, 1933.

In 1890, Dr. Westcott associated himself with Dr. Louis Starr and began to specialize in the diseases of children. He had numerous hospital and educational connections, all of which he had held many years. Among them were: assistant physician to the Children's Hospital of Philadelphia, 1895; visiting physician to the Methodist Episcopal Hospital, 1895; instructor in diseases of children, University of Pennsylvania, 1896, and associate in pediatrics, University of Pennsylvania, 1903.

Dr. Westcott wrote extensively in his earlier years. He was associate editor with Dr. Louis Starr in publishing "The American Text Book of Diseases of Children." Among outstanding monographs were: "Modified Milk and Percentage Milk Mixtures," and "The Scientific Modification of Milk" published in *International Clinics* in October, 1900.

Dr. Westcott was a Fellow of the College of Physicians and held memberships in the following societies: American Pediatric Society, Philadelphia County Medical Society, Philadelphia Pediatric Society, of which he was president in 1900, the Pathological Society, the Medical Club, the Physicians Motor Club and the Penn Club.

He was chairman of the Publication Committee of the College of Physicians for many years.

In 1893, Dr. Westcott married Marie Louisa Repplier. His wife and three daughters survive him.

W. N. B.

Abstracts from Current Literature

Anatomy and Physiology

INTRANUCLEAR AND CYTOPLASMIC INCLUSIONS ("PROTOZOAN-LIKE BODIES") IN THE SALIVARY GLANDS AND OTHER ORGANS OF INFANTS. SIDNEY FARBER and S. BURT WOLBACH, Am. J. Path. **8**:123 (March) 1932.

In the submaxillary glands of 183 infants intranuclear and cytoplasmic inclusion bodies were found in 22 cases, or 12 per cent. In addition, similar inclusion bodies were found in the parotid and submaxillary glands of 2 older patients, and in 2 instances in the liver, lungs, kidneys, pancreas and thyroid. All the patients were less than 17 months of age. The inclusions are apparently identical with those found in the submaxillary glands of guinea-pigs and generally similar to the inclusions found in filtrable virus diseases. There are no correlated clinical or pathologic findings. It is suggested that there may be geographic factors affecting the occurrence of these bodies, and that there is a disease in infants of filtrable virus etiology.

MOORE, Charlotte, N. C.

THE ROENTGENOLOGIC TECHNIC AND CHARACTERISTICS OF THE STOMACH OF THE NURSLING. E. CUMBO, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 847.

This is an essay covering the technic of roentgen examination and a discussion of the normal appearance of the infant's stomach in roentgenograms.

HIGGINS, Boston.

THE NORMAL RATE AND VOLUME OF THE CIRCULATION IN THE FIRST TWO YEARS OF LIFE. H. SECKEL, Jahrb. f. Kinderh. **131**:87 (March) 1931.

In fifty children under 2 years of age, the histamine rash method of S. Weiss gave a minimum time of circulation of from fourteen to seventeen seconds; in children over 2 years, a somewhat higher time; in adults, twenty-four seconds. The mean time is about double the minimum. Determination of the blood volume by the dye method permits the calculation of the circulatory volume per minute: infants, from 160 to 170 cc. per kilogram; children of 2 years, 130 cc. per kilogram; adults, 75 cc. per kilogram. The heart in infancy discharges from 5 to 18 cc. per beat.

CLAUSEN, Rochester, N. Y.

Pathology, Bacteriology and Biochemistry

EXPERIMENTAL OBSTRUCTIVE JAUNDICE: ITS EFFECT ON FIBRINOGEN AND COAGULATION OF THE BLOOD. WALTER MOSS, Arch. Surg. **26**:1 (Jan.) 1933.

The author attempted to find a scientific explanation of the hemorrhagic tendency in patients with jaundice. The diverse views expressed in the literature are reviewed. The fibrinogen content of the blood plasma was investigated from an experimental standpoint as a possible cause for this hemorrhage. Dogs were subjected to acute obstructive jaundice by dividing the common bile duct and accessory ducts between ligatures. Determinations of the fibrinogen in the blood plasma were made on the dogs that survived until jaundice developed. It was concluded from this experimental work that the fibrinogen content of the plasma is not decreased in experimental obstructive jaundice and that hemorrhage in the presence of jaundice is not due to a deficiency of this component of the plasma. It was also determined that the fibrinogen content of the plasma is increased in acute

obstructive jaundice, probably owing to the irritative effect of the bile on the liver. The author concluded that the coagulation time is not a satisfactory index of a hemorrhagic tendency in the presence of jaundice. KAISER, Rochester, N. Y.

EFFECTS ON COMPOSITION OF BLOOD OF PHYSIOLOGIC SOLUTION OF SODIUM CHLORIDE WHEN INTRODUCED BY INTRAPERITONEAL INJECTION AND BY STOMACH TUBE IN THE PRESENCE OF LOW BLOOD PRESSURE. J. W. BEARD, H. WILSON and ALFRED BLALOCK, Arch. Surg. **26**:122 (Jan.) 1933.

Studies were carried out in order to determine the effects of physiologic solution of sodium chloride when introduced by intraperitoneal injection and by stomach tube into animals with low blood pressure. Subcutaneous injection of histamine and graded bleeding were the methods used to produce low blood pressure. Introduction of physiologic solution of sodium chloride into the peritoneal cavity of the normal dog was associated with an increase in the volume of plasma, a slight dilution of the proteins of the plasma and a small increase in the absolute amount of plasma protein. When the blood pressure was caused to decline by the giving of histamine subcutaneously, there was a diminution in the volume of plasma and in the absolute amount of plasma protein. The removal of blood and the introduction of salt solution intraperitoneally were associated with decreases in the plasma volume and in the absolute amount of plasma protein. The findings in these experiments in which the fluid was introduced intraperitoneally were similar to those obtained following the subcutaneous injection of solution.

KAISER, Rochester, N. Y.

ABSORPTION OF DEXTROSE FROM THE COLON. WALTER W. EBELING, Arch. Surg. **26**:134 (Jan.) 1933.

The widespread use of fluids introduced through the rectum into the colon prompted the author to determine experimentally how much water and dextrose is actually absorbed by this method of injection. Experiments were conducted on dogs to determine if there is a marked difference in the ability of the ileum and of the colon of the dog to absorb dextrose. Dextrose solutions varying from 5 to 10 per cent were used, and the rate of absorption was observed for two hours. There was surprisingly little absorption of dextrose even when computed for a twenty-four hour period. There was slightly greater absorption when 10 per cent solutions were used. Tap water was found to absorb much more rapidly than dextrose solutions. The presence of dextrose in the solution in the colon, in the concentration used, actually caused a retardation in the rate of absorption of water.

This method of administration of fluid has little therapeutic value compared with subcutaneous or intravenous methods. KAISER, Rochester, N. Y.

OBSERVATIONS ON THE SEDIMENTATION TEST. A. R. HALPENNY, Irish J. M. Sc., January, 1932, p. 30.

The method of Fåhraeus was used, which is as follows: Into a tube 17 cm. long, with a 9 mm. bore, 2 cc. of 2 per cent sodium citrate is measured. Blood is put in to the 10 cc. mark. The tube is inverted and placed upright, and the rate of sedimentation is read in one hour. The Linzenmeier method measures the time required for the sedimentation to go a certain distance.

In normal subjects it was found that after one hour the red cells occupied 9.2 cc. or more. In conditions of breaking down of tissue the rate is increased. The author feels that the sedimentation test is not specific, but that it is of definite value as an indication of the amount of tissue breakdown, whatever may be the cause. SNELLING, Toronto, Canada.

A Contribution to the Study of Renal Function. T. W. T. Dillon and E. J. Conway, Irish J. M. Sc., March, 1932, p. 119.

The authors present a diffusion secretion theory of formation of urine with the clinical application for the determination of renal function. The equation, discovered by Austin and Van Slyke, which has been used as the urea clearance test of renal function, was applied by Conway to sulphate, sugar and chlorides, and found to hold. They introduced a correction into the formula for the weight of the patient, though they state that this is of theoretical importance, as it is clear that excretion of urea is a function of the body surface. In the test applied by them, urea is given to a nonfasting subject by mouth. A sample of blood and two specimens of urine were obtained at suitable intervals, and the urea in the blood and urine with its total volume was calculated. Graphs are given for normal subjects and for patients suffering from various types of renal disease. Renal function is estimated as a percentage.

Snelling, Toronto, Canada.

Disturbance in Osmotic Regulation in Experimental Dehydration. E. Kerpel-Fronius and F. Leövey, Arch. f. Kinderh. **94**:9 (July 17) 1931.

Exsiccosis was produced in young puppies by feeding milk concentrated to one-fourth its original volume. When signs of dehydration occurred, the animals were bled to death and chemical analyses were made of the blood and various internal organs. The osmotic pressure of the body fluids was greatly increased, and the residual oxygen and the chloride content were increased. In experimental uremia produced by ligating both ureters, the administration of sodium chloride exaggerated the symptoms and hastened death. It is likely that the high salt content and the increased osmotic pressure during exsiccosis exert a very injurious effect on the tissue cells.

LeMaster, Evanston, Ill.

Biologic Immunity of Pulmonary Inflammation: VI. Uniformity of Pneumonia in Infancy and Childhood. Eugen Kramár, Arch. f. Kinderh. **94**:81 (Sept. 11) 1931.

Pneumococcus vaccine injected intradermally into young puppies and guinea-pigs produced no reaction. However, when the injections were continued twice weekly, the animals soon responded with a severe cutaneous inflammation, showing a decided sensitivity to the pneumococcus. Continuations of the injections regularly through this period of allergic manifestations led to a third stage in which the animals again failed to show any obvious cutaneous reaction. Intratracheal instillation of living pneumococci had little effect on animals in the third stage of pneumococcus immunity, while all of the control animals died of sepsis. It is suggested that human beings exhibit varying degrees of susceptibility, allergy and immunity to the pneumococcus, as was manifested in the animals experimentally. The stage of immunity of the person determines to a great extent the particular types of pneumonia which he may contract. Senility or illnesses, such as measles and pertussis, may temporarily affect the immunity of a person, allowing so-called secondary pneumonia to appear. The different types of pneumonia are often not clearly distinct from each other because the various stages of immunity in patients are frequently transitional from one to another.

LeMaster, Evanston, Ill.

Nutrition

Nervous Manifestations in Infantile Scurvy. Orthello R. Langworthy, Bull. Johns Hopkins Hosp. **51**:117 (Sept.) 1932.

An undernourished child of 10 months on a diet consisting exclusively of milk showed definite signs of scurvy. After four days of dietary treatment and after two transfusions of blood had been given, a left hemiparesis, consisting of weakness of the facial muscles and the extremities on the left and loss of abdominal

reflexes and a positive Babinski sign on the left, developed. On the right side, there were tremors of the facial muscles and extremities.

At autopsy, the meninges, arteries and veins and cranial nerves appeared normal. There were multiple minute hemorrhages over the surface of the cerebellum. Sections of the brain showed numerous small hemorrhages from the rostrum to the genu, in the corpus callosum, almost exclusively to the right of the midline. There were numerous hemorrhages in the white matter of the right occipital lobe and a small hemorrhage on the right side of the floor of the lateral ventricle.

The author expresses the belief that the transfusions might have been an accessory factor in causing the hemorrhages in the nervous system.

LYTTLE, New York.

A COMPARATIVE STUDY ON THE USE OF UNSWEETENED EVAPORATED MILK AND BOTTLED COW'S MILK IN INFANT FEEDING. LILLIAN KOSITZA, J. Pediat. **1**:426 (Oct.) 1932.

Unsweetened evaporated milk was fed to 110 normal infants and 8 premature infants, while bottled cow's milk was given to 107 normal infants and 5 premature infants. Gain in height, constipation, frequency of infections and developmental points were almost identical for both groups. There was less diarrhea in the infants taking evaporated milk, but vomiting was more frequent at the onset. The weekly gain in weight was greater in the groups fed evaporated milk, but these infants received 5 calories per pound (0.5 Kg.) daily more than the group given bottled cow's milk. The author states that evaporated milk has the advantages of economy, availability, sterility, uniformity of composition and easy digestibility.

LEMASTER, Evanston, Ill.

THE ADVANTAGES OF EVAPORATED MILK IN ALLERGY AND INFANT FEEDING. JOHN B. ROSS, M. J. & Rec. **136**:276 (Oct. 5) 1932.

When cow's milk is evaporated under vacuum, 60 per cent of its water is removed. The fat globules are broken up by homogenization. After the milk is hermetically sealed in tins, it is sterilized, which removes all harmful bacteria from the tins. Homogenization and sterilization processes also serve to make the protein more digestible. Evaporated milk contains all the vitamins which bottled milk contains, except vitamin C. The author has used evaporated milk for the last three years with remarkable success in infants with symptoms of allergy, such as vomiting, eczema, colic, diarrhea, bronchitis, nervousness, restlessness, mucus in the stools and digestive disturbance. He also found advantages in it in feeding weak and premature infants. In conclusion he sums up the principal advantages of evaporated milk as follows: 1. It is easily digested. 2. It is safe, being sterile. 3. It may be given in concentrated form. 4. It is inexpensive and easily procured.

WILLIAMSON, New Orleans.

THE PLASMA PHOSPHATASE IN RICKETS AND SCURVY. JEAN SMITH AND MONTAGUE MAIZELS, Proc. Roy. Soc. Med. **25**:705 (March) 1932.

The authors first give a summary of the experimental work done on the enzyme known as phosphatase. Kay, applying this experimental work to clinical medicine, showed that certain generalized diseases of bone, such as osteitis fibrosa, osteitis deformans, osteogenesis imperfecta, osteomalacia and rickets, show an increase in this enzyme. A series of children with rickets were studied, and the course of the phosphatase content of the plasma and its healing process were traced. Later the study was extended to other conditions of which scurvy gave the most interesting results. The method taken in the study was that followed by Kay. The authors found that there is a high blood phosphatase content in rickets and a low one in scurvy, the explanation for which may lie in the

characteristic bone lesions in these conditions. It is believed that the high amount of plasma phosphatase is produced in attempted compensation for the bone lesion and the phosphatase content remains high long after serum calcium and inorganic phosphorus have returned to normal and even after roentgen examination has revealed normal bone formation. Whether these results can be put to any practical purpose in diagnosis and prognosis remains to be seen. It is clear that in considering the pathology of bone diseases, a third factor must be taken into account as well as the serum calcium and inorganic phosphorus, and this factor is subject to much wider variations from the normal than either of the latter two constituents of the blood.

WILLIAMSON, New Orleans.

THE ACTION OF VICHY WATER ON EXPERIMENTAL GLYCOSURIA AND HYPERGLYCEMIA. MAX VAUTHEY, Arch. d. mal. de l'app. digestif **22**:245 (March) 1932.

Rabbits were given subcutaneous injections of 5 Gm. of dextrose dissolved in 20 cc. of distilled water. There resulted a urinary excretion of from 4.5 to 5 per cent of the amount of dextrose injected. When the dextrose was dissolved in 10 cc. of distilled water and 10 cc. of Vichy water there was a decrease of 46 per cent in the amount excreted.

In the experiments on hyperglycemia the rabbits received 2 Gm. of dextrose per kilogram of body weight, the total amount being dissolved in 20 cc. of distilled water. The solution was given by mouth or subcutaneously to rabbits after a twenty-four hour fast. Blood sugar curves were plotted in the usual manner. After a week's rest the same animals were again, in a like manner, given similar doses of dextrose dissolved in 10 cc. of distilled water and 10 cc. of Vichy water. Blood sugar curves were again plotted, and were found to be neither so high nor so prolonged as in the experiments in which Vichy water was not used.

The author suggests that Vichy water may be of value in the treatment of diabetes mellitus.

TURNER, Chicago.

EXPERIMENTAL STUDIES ON THE RÔLE OF WHITE BREAD IN THE DIETARY. O. KAUFFMANN-COSLA and O. VASILCO, Arch. d. mal. de l'app. digestif **22**:261 (March) 1932.

If a dog is fed exclusively on white bread there occurs a serious nutritional disturbance, identical with that encountered in general avitaminosis, in insufficiency of vitamin B and in experimental scurvy. The administration of insulin has little effect in such a dog.

The authors conclude that white bread is not a complete ration.

TURNER, Chicago.

CHLOREMIA IN INFANTILE AZOTEMIAS. M. A. JAUREGUY AND W. AYALA, Arch. de méd. d. enf. **35**:339 (June) 1932.

The authors attempt to differentiate cases of azotemia in early childhood in which chlorides are indicated from those in which chlorides are interdicted. In the former the lesion is essentially renal, and the conventional treatment of reduced chlorides maintains the uremia; in the latter there is retention of chlorine, with nervous manifestations, probably due to infection or predilection in the cerebral tissues. Several case histories are offered to support these contentions.

AMESSE, Denver.

BERIBERI. J. ALBERT, Nourrisson **20**:169 (May) 1932.

Beriberi is responsible for 28 per cent of the deaths of babies under 1 year of age in the Philippine Islands. There are three clinical varieties: the atonic, the

pseudomeningitic and the cardiac. The last is the most serious type and is often fatal. The infants affected are usually between 3 and 6 months of age and are breast fed, the mother having beriberi in a mild form. The onset is sudden, the baby exhibiting signs of congestive heart failure and dying within twenty-four hours. Roentgen examination shows a dilated heart. Necropsy shows visceral congestion, dilated heart, especially of the right chambers, anasarca and degeneration of the vagus.

McCLELLAND, Cleveland.

IS HYPOPHOSPHATEMIA THE ESSENTIAL BLOOD STIGMA IN RICKETS? A. B. MARFAN, Presse méd. **40**:561 (April 13) 1932.

Marfan reviews the theories of the relation of hypophosphatemia to rickets which have been propounded since 1919, when Iversen and Lebstrup discovered that the inorganic blood phosphorus is lowered in rickets. It was held for some time that there was a direct connection between the hypophosphatemia and the degree of rickets. This was refuted by Dollencourt and Spanien in 1924. In 1930, Hess declared that hypophosphatemia is not an essential feature of the pathology of rickets.

There has been much controversy over the connection between the acidosis often found in rickets and hypophosphatemia. The two conditions so often exist independently of each other that it is impossible to draw definite conclusions. The frequent occurrence of hyperphosphatemia in rickets complicated by tetany suggests that an excessive proportion of phosphorus is responsible for this complication. As there is often alkalosis accompanying tetany, this suggests that there is a link between acidosis and hypophosphatemia and alkalosis and hyperphosphatemia. These factors are too variable for conclusions. It can only be stated that in infantile tetany hypocalcemia usually coincides with an increased amount of inorganic blood phosphorus. These facts cannot be explained in the light of present knowledge.

BIEKER, St. Petersburg, Fla.

SULPHUR COMPOUNDS AND GROWTH. L. BINET AND J. MAGROU, Presse méd. **40**:853 (May 28) 1932.

The relation of the amount of sulphur in the young animal or plant to its growth has aroused considerable interest in recent years. Two matters command attention: first, the elevated content of glutathione in the tissues of the young; second, the influence of the experimental administration of sodium hyposulphite on growth.

In young rats the glutathione content of the liver tissue at birth is 666 mg. per hundred grams; at 26 days it is 344 mg., and at 66 days, 210 mg. Experiments were conducted which showed that the germination and growth of certain grains were distinctly hastened by treatment with 1:1,000 solution of sodium hyposulphite (this concentration was determined to be the optimum), and that the metamorphosis of tadpoles was greatly hastened by the addition of 1 part sodium hyposulphite to 1,000 parts of the water in which they were kept.

BIEKER, St. Petersburg, Fla.

THE EVOLUTION OF THE PATHOLOGIC CONCEPTION OF CRANIOTABES. M. SCHACHTER, Progrès méd., June 25, 1932, p. 1138.

The author traces conceptions of craniotabes from Vimont's first description, in 1833, to those of the present. The early writers always considered craniotabes to be rachitic or syphilitic in origin. Later it was decided that two forms could exist: a true congenital and an acquired form, i. e., rickets and osteogenesis. Pressure was thought to be a prominent cause in the congenital type, but prenatal influences only were involved. Abels offered in favor of this the observation that it was found more often in first children, rarely in the premature and

never in children born by breech presentation. Jundel, in 1931, finally cleared up the question by showing that craniotabes was simply a phenomenon of mechanical pressure on the cranium, which caused osseous plaques of hyperplasia on the regions involved, thus arresting the ossification in the region exposed to this pressure.

SANFORD, Chicago.

IRON IN INFANT NUTRITION. A. WALLGREN, Rev. franç. de pédiat. **7**:257 (Oct.) 1932.

The author found the iron in mothers' milk to average 0.437 mg. a liter, in goats' milk, 0.356 mg., and in cow's milk, 0.239 mg. In cheese it varied greatly according to the way and the part of the country in which it was made. In French cheese the iron content varied from 0.004 to 0.24 mg. in a gram. In cereal the content of iron depends greatly on whether it is whole cereal or not. In milled rice the iron content averages only 0.0067 mg. per gram while whole rice averages 0.109 mg. Of the breadstuffs graham bread has the highest iron content, averaging 0.059 mg. in a gram. Among the fruits, the iron content in cherries averages 0.0038 mg. in a gram, while that of black raisins with pips is 0.0032 mg. In the vegetables, the content of spinach averages 0.054 mg. in a gram. In cocoa, which is classed as of vegetable origin, the surprising amount of 0.744 mg. a gram is found. Beef is the meat with the content highest, there being 0.024 mg. in a gram; in eggs there is 0.0482 mg., and in blood pudding, 0.212 mg. a gram.

SANFORD, Chicago.

A PLEA FOR RAW MILK. C. COHEN and G. RUELLE, Rev. franç. de pédiat. **7**:312 (Oct.) 1932.

The authors have collected a considerable number of articles, and they present the histories of eight cases in which the patients appeared to improve markedly when raw milk was given. They contend that there is some growth-promoting property that is destroyed by boiling. They admit, however, that raw milk must be obtained under ideal conditions, namely, a clean animal, bacteria-free, and milk collected in a sterile container and kept free from bacteria throughout handling.

SANFORD, Chicago.

BLOOD CONCENTRATION AND WATER METABOLISM IN CHILDHOOD. S. PAULON, Riv. di clin. pediat. **29**:1115 (Dec.) 1931.

The author found that the maximum dilution of the blood following the drinking of water by children occurred in forty minutes.

From observations on fifty children who had taken by mouth 10 Gm. of water per kilogram of body weight he found that in forty minutes the refractive index of the blood had fallen from 1.3520 to 1.3505, indicating a fall in albumin content from 9.31 to 8.44 per cent; the water of the blood had increased from 80.963 to 82.254 per cent; of the 10 Gm. taken in, 4.48 Gm. had been excreted by the kidneys, 0.98 Gm. had remained in the blood and 4.54 Gm. had been taken care of by other means of excretion, such as skin and lungs. These figures should serve as normal values for evaluating the findings in abnormal patients.

HIGGINS, Boston.

THE QUANTITIES OF INORGANIC PHOSPHORUS AND OF TOTAL ACID-SOLUBLE PHOSPHORUS IN SERUM AS AFFECTED BY ULTRAVIOLET IRRADIATION IN VITRO. A. COLONNA, Riv. di clin. pediat. **30**:71 (Jan.) 1932.

In sixteen of twenty-four cases in which the blood serum of children was irradiated in vitro, there were an increase of the inorganic phosphorus of the blood and a corresponding decrease in the acid-soluble phosphorus.

HIGGINS, Boston.

SOME PHYSICOCHEMICAL CONSTANTS OF THE FAT OF WOMAN'S MILK AND THEIR RELATIONS TO EACH OTHER. MARTA RADICI, Riv. di clin. pediat. **30**:756 (June) 1932.

The following constants of the fat of twenty samples of human milk were determined: percentage of fat, melting point, iodine content, number of fat globules per cubic millimeter of milk and percentages of large, medium-sized and small globules.

The larger the number of fat globules per cubic millimeter, the higher was the percentage of fat in the milk, while usually the higher the percentage of fat, the higher the percentage of large fat globules.

There was no relation between the melting point or iodine content and the percentage of fat.

Usually a low melting point means a high iodine content.

HIGGINS, Boston.

INFLUENCE OF ULTRAVIOLET RAYS ON "THIEMIA." E. INGLESSI, Riv. di clin. pediat. **30**:1141 (Sept.) 1932.

By "thiemia" is meant the total nonprotein sulphur of the blood. This may be divided into two parts, the oxidized sulphur and the neutral sulphur. The oxidized sulphur represents a metabolic end-product of ingested protein, while the neutral sulphur represents an end-product of catabolism of tissue protein.

The author determined the sulphur of the blood before and after the irradiation of rabbits. Short periods of irradiation (five, eight or ten minutes) diminished the total sulphur of the blood, but increased the ratio of oxidized sulphur to total sulphur.

Longer periods of irradiation (fifteen, thirty or forty-five minutes) increased the total sulphur, but decreased the ratio of oxidized sulphur to total sulphur.

HIGGINS, Boston.

INTOXICATION AND DEHYDRATION. ARNOLD ORGLER, Jahrb. f. Kinderh. **135**:147 (April) 1932.

Cases of alimentary intoxication are described (*a*) in which the symptoms disappeared although the body weight did not rise and (*b*) in which, after the usual rise in weight, a marked fall was observed with no reappearance of symptoms. The author believes that dehydration alone does not explain intoxication, and that one of the factors in the causation of intoxication is pathologic displacement of water within the body.

CLAUSEN, Rochester, N. Y.

BASAL METABOLISM DURING FEVER. B. ESSIG, Monatschr. f. Kinderh. **53**:335, 1932.

In infections of considerable duration, such as the vaccinia following smallpox vaccination, there is a definite increase in metabolism during incubation and through the febrile period, and then a secondary increase after subsidence of the fever. Unquestionably the same holds true in conditions such as measles and chickenpox. The present study was made on conditions having a short or no period of incubation such as the usual grippal infections. In these the rise of metabolism does not occur until the definite rise in temperature. The metabolism then sinks gradually, even though fever persists. It reaches normal about the time that the temperature in a more abrupt descent has also become normal. In long-continued fever, such as in chronic infections, the metabolism is likely to be high at the beginning and gradually fall to subnormal. This the writer interprets as being due to the malnutrition resulting from the chronic loss of appetite; in a case described it was advised to keep the metabolism high by continuing a plentiful diet.

The fact that in fevers of short duration the metabolism starts dropping before the temperature suggests that the temperature is not due to increased heat production but to diminished heat loss.

GERSTLEY, Chicago.

BASAL METABOLISM IN ATROPHIC INFANTS. B. ESSIG, Monatschr. f. Kinderh. **53**:343, 1932.

Fifty-six determinations were made in nine atrophic infants. The weight varied from 29 to 48 per cent below normal. Six premature infants were also studied. Essig found that the metabolism of the individual child remained constant, but there were decided variations between the different children. As a working rule the best method of estimating metabolism is through the weight. The greater the deficiency in weight of the infant, the more do the figures for metabolism differ from the normal. The lowest metabolism occurs in the group of the smallest infants, whose weight during the third and fourth weeks varied from 1,500 to 1,900 Gm. With a weight of over 2,000 Gm. and an age of from 7 to 9 weeks, the metabolism rose from 44 calories per kilogram to from 53 to 61 calories per kilogram. But even in infants of from 3 to 4 months of age, values as low as from 43 to 48 calories per kilogram were found.

GERSTLEY, Chicago.

INTOXICATION IN ANIMALS INDUCED BY FEEDING. ALICE CHASSEL and S. ROSENBAUM, Monatschr. f. Kinderh. **53**:399, 1932.

Rosenbaum in previous experiments showed that alimentary intoxication could be induced in dogs by the combined effects of dehydration and parenteral administration of bacterial endotoxins. Further work showed that amines could be substituted for the endotoxins.

The present experiments, undertaken with fifty-five experimental dogs and eighteen controls, were devised to see if endotoxins could be given by mouth to produce similar effects. Large amounts of coli endotoxin were given by mouth with no results. Injection of the same cultures into the intestine provoked no response. The growth of colon bacilli in mediums designed to increase the production of amines was next tried, but this likewise had no effect when given by mouth. Most of the animals died, but without the symptoms of alimentary intoxication. Production of injury to the intestine, which theoretically would facilitate absorption of these mixtures, did not produce the syndrome.

When amines themselves were given enterally, however, to dehydrated animals the syndrome of alimentary intoxication developed in six of ten. These experiments are of definite significance in that one hundred times the ordinary amount of bacterial endotoxin, which produced results when given parenterally, had no effect when given by mouth.

The writers leave the question open as to whether or not these results are applicable to infants.

GERSTLEY, Chicago.

DEHYDRATION IN ANIMALS ON A DRY PROTEIN-FREE DIET. ROSENBAUM, Monatschr. f. Kinderh. **54**:245, 1932.

It has been experimentally established that a certain amount of protein in the diet demands a certain minimum of water. When the intake of water falls below this minimum ratio, fever results. In view of these observations, the author wished to study the effect of dehydration in animals on a diet low in proteins. Animals were fed diets containing a minimum of protein with little water and kept in warm surroundings.

It was found that there was little difference in the reaction between the animals on diets with protein and those on diets without it. The two series showed identical reactions to dehydration, such as the concentration of the blood and

the diminution in the water, fat and glycogen content of the liver. In neither series was there a special diminution in the water content of the portal region, as has been described by others.

In the dogs on the protein-free dry diet a state of "intoxication" could be produced by the administration of endotoxins or amines, just as in the other group.

GERSTLEY, Chicago.

CHEMICAL COMPOSITION OF THE TISSUE OF THE NURSLING. VON MORITZ, DENES and KERPEL-FRONIUS, Monatschr. f. Kinderh. **54**:371, 1932.

In a study of the organs of fifteen nurslings dying of various diseases, the authors determined the osmotic pressure by means of the freezing point, as well as the chlorine, the nonprotein nitrogen and the water content. In two cases of acute loss of weight with dehydration, the tissues showed evidences of hyperosmotic values, but these were by no means as great as those produced experimentally in animals. The increased osmotic pressure in infants cannot be due entirely to the drying of the tissues, for the water content was only moderately diminished. Probably changes in the nitrogenous residues are of as great importance as the diminution of the water content.

The authors also describe a case of loss of weight in which the essential factor seemed to be a great outpouring of chlorine.

GERSTLEY, Chicago.

INFLUENCE ON RICKETS OF IRRADIATION OF SKIN AREAS OF VARIOUS SIZES. W. CATEL, Monatschr. f. Kinderh. **54**:426, 1932.

While no one questions the influence of ultraviolet radiation on rickets, no one has determined the minimum area of skin which must be irradiated in order to secure beneficial results. Studies were made on serum calcium and phosphorus; roentgenograms and clinical observations were used as controls. In four nurslings an area of 9 sq. cm. was irradiated over a period of from three to six weeks. In another group the area was increased to 90 sq. cm. In a third group, the whole face was exposed, the eyes being protected. In a few cases an effort was made to irradiate the mucous membrane of the lips in order to determine the effect of irradiation of the mucosa.

The results show that the children whose faces were irradiated made a complete recovery in four weeks. Irradiation of the small areas of mucosa or of 9 sq. cm. of skin was valueless.

The writer concludes from these experiments that it is unnecessary to undress the child, provided a sufficient area of the face is exposed to sunlight.

GERSTLEY, Chicago.

IS SOY BEAN FLOUR AN ANTIRACHITIC SUBSTANCE. HANS BISCHOFF, Monatschr. f. Kinderh. **54**:435, 1932.

As soy bean flour contains a large percentage of phosphorus, the writer undertook experiments to determine whether it had an antirachitic effect. In experiments on rats it was found that the addition of soy bean flour in amounts from 1 to 16 per cent to a rachitic diet had no effect. When the amount of flour was increased to 50 per cent, the rickets was cured.

GERSTLEY, Chicago.

IRON METABOLISM IN PREMATURE INFANTS. O. BECK, München. med. Wchnschr. **79**:378 (March 4) 1932.

This study of the iron metabolism in premature infants was made at the Childrens Hospital of Cleveland. Beck used a new method which enabled him to make his metabolic studies without exposing the infants to chilling and other

dangers that former methods entailed. The first series of observations calls attention to the uniform and rapid decrease in both the hemoglobin and red blood cells in premature infants while they are making a satisfactory and steady gain in body weight. The amount of excreted iron was then measured. During the first few days the excretion was low, namely, 1.2 mg. There was a gradual increase until the maximum excretion was reached, on from the thirty-fifth to the fortieth day. Following this peak there was a gradual decrease until a rate of excretion was reached that was lower than that during the first few days of life. Another series of premature infants was given 0.2 mg. of iron daily in addition to their formula for fourteen days. The amount of iron excreted was then measured during this period and for the following two weeks. During the period that the iron was administered there was a slight increase in the iron retention. However, during the following two weeks approximately all the iron that was originally retained was excreted.

Clinically Beck found that the feeding of either iron alone or vitamin C alone did not influence the anemia of premature infants. When a combination of iron, orange juice and lemon juice, however, was fed to children, there was an improvement. Unfortunately no further metabolic studies could be made.

BRAHDY, Mount Vernon, N. Y.

CLINICAL AND PATHOLOGIC OBSERVATIONS ON ACETONEMIC VOMITING OF CHILDREN. L. SALOMONSEN and H. BJELKE, Ztschr. f. Kinderh. **53**:66, 1932.

The authors describe a case of a young boy who, during bouts of vomiting, had signs and symptoms of angioneurotic edema and other manifestations of allergy. It is suggested that the attacks of vomiting are due to the reaction of the gastrointestinal tract to some foreign substance in the same manner as the respiratory system reacts in asthma.

The effects of epinephrine and insulin on blood sugar and acetone bodies were studied in a group of children subject to attacks of vomiting and also in normal children after fasting and after diets high in fat. There was no great difference in the response to these agents between the normal children and those subject to vomiting, which indicates no disturbance in hepatogenic or glycogenic function. In contrast to the hypoglycemia reported in patients with cyclic vomiting, the values for blood sugar during fasting in the cases studied were within normal limits.

SHELLING, Baltimore.

VARIATIONS OF THE MAGNESIUM CONTENT AT DIFFERENT AGES, ESPECIALLY IN RICKETS AND TETANY OF CHILDREN. E. KRUGER, Ztschr. f. Kinderh. **53**:83, 1932.

The magnesium concentration of the blood serum was found to vary quite markedly. Nurslings show the highest values for serum magnesium and older children the lowest; they are again higher in adults. In infantile rickets the magnesium content in the blood serum is about 50 per cent of the normal; in healing rickets and rickets complicated with tetany the values are higher than in rickets or approach normal.

SHELLING, Baltimore.

EXPERIMENTAL OBSERVATIONS ON THE EXCRETION OF CALCIUM, PHOSPHORUS AND CARBON DIOXIDE AFTER OVERDOSAGE WITH VIOSTEROL. J. WAKARNY and A. WASITZKY, Ztschr. f. Kinderh. **53**:171, 1932.

The feedings of large doses of viosterol to rabbits subsisting on greens produces an increased excretion of phosphorus in the urine. The calcium and carbon dioxide of the urine show no definite changes except for a tendency to decrease.

SHELLING, Baltimore.

APPLE TREATMENT OF ACUTE ENTERITIS IN CHILDREN. N. ASAI, J. Pediat. (Tokyo), May 20, 1932, no. 384, p. 912.

The author used ripe grated apple in thirty cases of acute enteritis in children between the ages of 1 and 4 years. He followed the method of Moro, but instead of using the apple for only two days, he continued its use after the institution of the fluid or semisolid diet after the third day of illness. He found that the use of grated ripe apple at the beginning of the illness contributed greatly to speedy recovery, with a fall in temperature and cessation of the more severe symptoms of vomiting and pain. The author, however, is unable to state positively that the apple was solely responsible for the favorable course of the disease in these cases.

KATO, Chicago.

THE ACTION OF VITAMIN E. F. VERZAR, Magyar orvosi arch. **32**:273, 1931.

Female rats were fed on a vitamin E-free diet. Long before absorption sterility sets in, the rats show changes in their behavior toward their young. Their first litter is fed, but none after that. This second generation does not rear any of its young. Lack of vitamin E manifests itself in the mother and not in the embryo. Wheat-germ extracts containing vitamin E, like the sexual hormone of the anterior lobe of the hypophysis, cause a hypertrophy of the uterus of infantile but not of castrated rats. Characteristic changes take place in the hair of male rats fed on a vitamin E-free diet. The hair which is normally coarse becomes soft and cotton-like. This, too, is the case with hypophysectomized rats. Lack of vitamin E disturbs the production of sexual hormones, particularly that of the anterior lobe of the hypophysis. KUGELMASS, New York.

Diseases of the New-Born

ERYTHROBLASTOSIS FETALIS AND ITS ASSOCIATION WITH UNIVERSAL EDEMA OF THE FETUS, ICTERUS GRAVIS NEONATORUM AND ANEMIA OF THE NEWBORN. LOUIS K. DIAMOND, KENNETH D. BLACKFAN and JAMES M. BATY, J. Pediat. **1**:269 (Sept.) 1932.

The authors review the literature on universal edema of the fetus, icterus gravis neonatorum, erythroblastosis fetalis and anemia of the new-born. Twenty cases are discussed with reference to history, physical findings, laboratory data, pathologic changes and differential diagnosis. The points of similarity are carefully and fully pointed out, showing that they are closely related. Each symptom complex is portrayed as a part of a sequence dependent on the severity and duration of the disease. It is suggested that these conditions are all due to the same underlying pathologic process. Twelve case reports are presented in detail.

LEMASTER, Evanston, Ill.

EXFOLIATIVE DERMATITIS IN THE NEW-BORN (RITTER'S DISEASE). G. L. HALLEZ, Nourrisson **20**:270 (Sept.) 1932.

This disease is not to be confounded with dermatitis desquamativa (Leiner's disease). The former was described by Ritter in 1878; the latter by Leiner in 1907. Many authors still deny their duality. The exfoliative dermatitis always appears in new-born infants between the ages of 6 and 35 days. The lesions appear as red spots on the face, particularly around the mouth and on the chin; thence the involvement spreads rapidly so that in two or three days the skin of the entire body is affected. The extremities in some cases are spared. The original lesions quickly turn to vesicles and the bullae are filled with a cloudy serum. Detachment of the epidermis in lamellae quickly follows so that large areas are denuded, giving the baby the appearance of having been scalded. In rare cases,

lesions appear in the nose and mouth and on the cornea. The mortality is at least 50 per cent. The most common micro-organism cultivated from the lesions has been the staphylococcus.

McCLELLAND, Cleveland.

ICTERUS NEONATORUM. KURT SAMSON, Kinderärztl. Praxis **4**:168 (April) 1932.

The present state of knowledge of simple icterus neonatorum is as follows: The increased volume of blood in the new-born is broken down in a short time into bilirubin which is transferred to the blood stream by an extrahepatic route (as shown by the negative Diazo reaction) and does not appear in the urine. A temporary functional insufficiency of the liver may cause the bilirubin to remain for a long time in the blood stream and give it an opportunity to penetrate the skin. However, the endothelium of the capallaries of the skin is partly responsible for the severity and continuance of the icterus. The volume of blood in the new-born is increased because the fetus lives in a milieu poor in oxygen, and as soon as extra-uterine life makes this compensation mechanism unnecessary, the superfluous amount of blood is broken down.

In icterus gravis conditions are different. There is anatomic evidence of definite changes in the liver, the Diazo reaction appears at once and bilirubin appears in the urine. There is a definite erythroblastosis as an expression of the disturbance of the equilibrium in the building up and breaking down of the blood. This is not a physiologic process, but a severe disturbance, in which the changes in the liver play an important though not the primary rôle.

HUENEKENS, Minneapolis.

A STUDY OF BACTERIOPHAGE IN THE STOOLS OF THE NEW-BORN INFANT. T. TOMOISHI, J. Pediat., Tokyo, Nov. 20, 1932, no. 390, p. 2124.

The author made sixty-eight examinations of stools from twelve new-born infants, and demonstrated 7.5 per cent positive tests, as against 16 per cent reported by Suranyi-Kramar. The earliest stool in which bacteriophage was positive was on the fourth day. No positive results were obtained in the meconium. The most pronounced phage effect was seen against B. paradysenteriae (Mita), and then against atypical and typical dysentery bacilli; the least was seen against B. coli and B. typhosus. No phage effect was seen against B. paratyphosus.

KATO, Chicago.

Acute Infections

GENERALIZED VACCINIA: REPORT OF CASE OF TRUE VACCINIA. S. W. MARICK, Arch. Pediat. **49**:552 (Aug.) 1932.

A case of hematogenous, or metastatic, vaccinia is reported. The differential diagnosis is discussed and possible causes of true vaccinia analyzed.

WADDELL, University, Va.

TICK-BITE FEVER IN CHILDREN. P. G. SHIPLEY, Bull. Johns Hopkins Hosp. **51**: 83 (Aug.) 1932.

A brief review is made of the typhus-like fevers in the United States. Tick-bite fever of the coast was identified in Maryland in 1929 and is apparently increasing. Neither sex and no age is immune. The vector is the ordinary wood or dog tick (Dermacentor variabilis). The results of experimental studies on animals are given.

Clinically, there is a history of exposure and a short incubation period, usually from two to five days. The onset is accompanied by fever, drowsiness, headache and vague pains. Gastro-intestinal symptoms are absent. The severe form resembles European typhus, with stupor, delirium and motor activity. The eruption is generalized, and the fever is continuous, terminating by a rapid lysis. In mild

cases the patients may show only apathy, a few spots and fever. The eruption is at first rose-colored and macular; it appears from the third to the fifth day, first on the extremities, and becomes thickest on the areas subject to pressure; the face is usually not involved. Later, the rash tends to coalesce and become hemorrhagic. A scaly desquamation follows. An equivalent enanthem is present.

The differential diagnosis is between typhoid and typhus. The Weil-Felix reaction may help in the diagnosis.

Treatment is prophylactic, and the prognosis for children is favorable.

LYTTLE, New York.

PSEUDO-SCHICK REACTION AND DIPHTHERIA CARRIERS. FERDINAND HERB, M. J. & Rec. **136**:222 (Sept. 21) 1931.

The Schick reaction is due, as are all other tests of the skin, to the development of poisonous bodies at the place of the injection. These poisonous substances originate during the parenteral digestion of the specific antigen. This digestion is accomplished by ferments, and these ferments require the assistance of a complement. If there is a sufficiency of both of these substances, the specific antigen is so quickly broken down into harmless end-products that the poisonous intermediary split-products do not exist long enough to harm the tissues, and there are no inflammatory symptoms in the skin. The test is negative. If there is an insufficiency of ferments, the intermediary poisonous split-products remain long enough in the tissues to set up an inflammation; this is known as a positive Schick test. The pseudo-Schick test is caused by insufficiency of the complement. The characteristics of differentiation between these two positive reactions are in the pseudoreaction. The inflammatory symptoms appear within from six to twelve hours, and disappear about the third or fourth day. The true reaction develops more slowly, reaching its height about the third or fourth day. It may last for a whole week and then fade slowly. In conclusion, the author shows the connection which exists between the pseudo-Schick test and carriers.

WILLIAMS, New Orleans.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, SEPTEMBER 11 TO OCTOBER 8, 1932. Pub. Health Rep. **47**:2105 (Oct. 28) 1932.

Although the incidence of poliomyelitis remained about the same as during the previous four week period, it was substantially lower than at the same period, during previous years. Scarlet fever increased more than 50 per cent and influenza more than 40 per cent over the preceding four week interval.

Cases of smallpox, typhoid fever and meningococcic meningitis continued to decrease, the number of cases being much lower than in the past years. A normal seasonal increase occurred in diphtheria, while the incidence of measles remained about the same. The mortality from all causes in large cities continued to be low, there being 9.5 deaths to a population of one thousand persons.

LEMASTER, Evanston, Ill.

AN ALLERGIC SKIN REACTION AFTER SCARLET FEVER. H. J. GIBSON and J. P. MCGIBBON, Lancet **2**:729 (Oct. 1) 1932.

In twenty-eight cases of scarlet fever, weekly intracutaneous tests were carried out with an extract prepared from cultures of hemolytic streptococci representing the soluble intracellular products of the organisms freed from diffusible substances. The extract was diluted 1:100 for the test.

In twenty-two patients the reaction, which was negative during the first week, became strongly positive by the fourth week.

The clinical significance of the development of this highly allergic state in the late stages of scarlet fever is difficult to ascertain. Of many patients who acquire specific hypersensitiveness as a result of scarlatina, few subsequently show evidence of the rheumatic syndrome.

LANGMANN, New York.

TWO CASES OF PARALYSIS OF THE OCULOMOTOR NERVE FOLLOWING THE PREVENTIVE INJECTION OF ANTITETANIC SERUM. VALERIO, Arch. d'opht. **49**: 181 (March) 1932.

The author records two observations of complete paralysis of the oculomotor nerve following a second injection of antitetanic serum. This serum acts as a true poison, much like nicotine, alcohol, etc., leading to an intrafascicular edema which interrupts the function of the nerve. These paralyses are relatively rare and do not imply the need of restriction in the use of the serum. Both the patients observed recovered completely after a month through the use of diathermy. According to the author, simple edema is the most rational explanation for the occurrence of this condition.

MARLOW, Syracuse, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

SOME SEQUELAE OF TETANUS. D. MUELLER and A. QUÉNÉE, Paris méd. **22**: 273 (Oct. 8) 1932.

The sequelae are due to a destruction of body cells by the toxin of tetanus and involve not only the nervous system, but the muscular and osseous systems as well. The osseous pathologic process seems to be an osteoporosis. The authors recommend a thorough examination following tetanus.

SANFORD, Chicago.

INFECTIOUS ERYTHEMA (FIFTH DISEASE). P. MEYER, Rev. franç. de pédiat. **7**: 363 (Oct.) 1932.

The author describes a case in a child of 2 years. The incubation period is seventeen days. The prodromal stage is three days. The symptoms are the appearance of erysipeloid, red, erythematous patches on the face and body. There is no pain or fever. The leukocyte count is usually elevated to 14,000. There is no treatment except rest.

SANFORD, Chicago.

OPIATES IN THE TREATMENT OF CHILDREN, WITH PARTICULAR REFERENCE TO LARYNGEAL DIPHTHERIA. A. GALEOTTI-FLORI, Riv. di clin. pediat. **30**:508 (April) 1932.

The author made observations on twelve children and infants without acute infections following the injection of morphine and papaverine; the pulse rate, the respiratory rate and the blood pressure, as well as other pharmacologic symptoms, were recorded. Similar observations were made on patients given these drugs during the treatment of acute laryngeal diphtheria.

The author concludes that these two alkaloids of opium are well tolerated by children.

HIGGINS, Boston.

AMEBIC CYSTITIS IN CHILDREN. S. MOSCHINI, Riv. di clin. pediat. **30**:648 (May) 1932.

Amebic cystitis of children is usually secondary to amebic dysentery, and occurs almost wholly in girls. In the case reported, however, the patient, a girl 3 years old, had no dysentery, and amebas were not found in the stools, sputum or teeth. The patient was recovering from typhoid fever with some bronchial complications. After five days of normal temperature, a routine examination of the urine showed 500 cc. in twenty-four hours, an acid reaction and albumin, but no blood, sugar, acetone or bile. In the sediment were found many epithelial cells, no red cells, occasional clumps of white cells and numerous amebas.

The pyuria increased on later examinations. Culture of the urine gave negative results for B. coli and B. typhosus.

Treatment with methenamine did not make an appreciable change in the urinary sediment, even after one month. Then treatment with emetine hydro-

chloride was instituted; eight injections of 1 cg. of emetine hydrochloride cleared up the cystitis.

The author believes that the amebas found are of the type Entamoeba vesicalis.

HIGGINS, Boston.

STUDY OF THE SCHICK TEST AND OF PROPHYLACTIC ANTIDIPHTHERITIC VACCINATION. V. SAGGESE, Riv. di clin. pediat. **30**:865 (July) 1932.

Of 347 Schick tests made by the author on Italian children in Pisa, 158, or 45 per cent, were positive.

In an institution, he was able to perform Schick tests on 25 mothers and their children under 6 months of age. Both mother and child gave positive reactions in 2 cases and negative reactions in 13 cases. The mother's reaction was positive and that of the child negative in 8 cases, while the mother's reaction was negative and the child's positive in 2 cases.

In the author's cases nasal insufflation of Ramon's anatoxin was not successful in producing permanent immunity (a negative Schick test after from six to eighteen months). Four of thirteen children had a negative Schick test, seven a positive test and two a doubtful positive six months after this treatment. In similar observations made on twenty-two children, when the anatoxin was given hypodermically, only one child had a positive Schick test from four to six months after the prophylaxis was completed.

Repeated Schick tests occasionally immunize a child against diphtheria.

HIGGINS, Boston.

SEVERAL UNUSUAL CASES OF EPIDEMIC CEREBROSPINAL MENINGITIS. A. PICCIOLI, Riv. di clin. pediat. **30**:1249 (Oct.) 1932.

Five cases of meningococcic meningitis are reported. In case 1, hydrocephalus developed in an infant of 8 months who had had a prolonged subacute illness.

In case 2, that of an infant only 18 days of age, the youngest on record, the disease was characterized only by fever and irritability for nine days. Then the first symptoms of cerebral involvement appeared, and convulsions occurred. The child died one month after the onset of symptoms.

In case 3, a child of 2½ years showed encephalitic as well as meningeal, symptoms. Definite signs of intracranial pressure were present.

In case 4, a child of 26 months was an ambulatory patient with meningitis for probably three months before treatment was begun.

In case 5, a child of 3 years had a mixed infection of the meninges; both meningococci and pneumococci were found in the spinal fluid.

HIGGINS, Boston.

SCARLET FEVER AND SCARLATINIFORM EXANTHEMAS FROM SERUM. THE VALUE IN DIFFERENTIAL DIAGNOSIS OF THE INTRADERMAL REACTION TO HORSE SERUM. P. COCCHERI, Riv. di clin. pediat. **30**:1276 (Oct.) 1932.

In 1904, Marfan described a complication appearing in patients with diphtheria, which he called *"scarlatinoïde metadiphtérique"*; it was characterized by fever and a scarlatiniform eruption. On the basis of clinical and laboratory observations Coccheri has come to the conclusion that Marfan's metadiphtheria was real, but atypical and attenuated, scarlet fever.

Another scarlatiniform eruption appearing in diphtheritic patients is caused by serum. The differential diagnosis between the two conditions, scarlet fever and serum sickness, is discussed at some length.

The clinical points of differentiation depend on: (1) the immunity of the patient; that is, the history of a previous attack of scarlet fever; (2) the existence of an epidemic of scarlet fever in the vicinity or the exposure of the patient to the disease; (3) the time of eruption after the serum is given; a serum rash is most commonly seen on from the seventh to the twelfth day, but it may appear

as early as the second and as late as the seventeenth day; (4) the fact that serum rashes are most marked at the site of injection; (5) a more definite enanthem in scarlet fever; (6) a localized cervical adenitis in scarlet fever, as compared to a generalized adenopathy in serum reactions; (7) a more evident icteroid tint to the skin is scarlet fever; (8) usually more marked desquamation in scarlet fever, and (9) the complications, such as suppurative lesions and nephritis, following scarlet fever and immediate albuminuria or edema, as of the larynx, indicating a reaction to serum.

The laboratory points of differentiation are as follows: 1. The presence of urobilin and of acetone bodies is more likely to occur in scarlet fever. 2. Leukocytosis and eosinophilia are more marked and continued in scarlet fever than in reactions to serum. 3. A blanching test gives positive results in scarlet fever and negative ones in a reaction to serum. 4. A positive reaction to horse serum suggests serum sickness. In scarlet fever the intradermal test is always negative, except in cases in which sensitivity to horse serum preceded the injection of the diphtheritic antitoxin.

In serum rashes the intradermal test is always positive in the early stages and usually positive at the height of the eruption, and it is doubtful or negative as the eruption fades and immediately thereafter.

HIGGINS, Boston.

ANTIDIPHTHERITIC VACCINATION. RESULTS AND DEDUCTIONS FROM THE SCHICK TESTS IN SEVERAL INSTITUTIONS IN FLORENCE. V. PINTOZZI, Riv. di clin. pediat. **30**:1318 (Oct.) 1932.

Of 1,827 Schick tests made, the results in 752, or 41 per cent, were positive; those in 107 were only slightly positive; those in 494 were moderately positive, and those in 151 were markedly positive. Usually the positive tests were less intense in infants than in older children.

The percentage of positive tests grouped according to the age of the subject are given in the following table:

Age	Positive Tests, per Cent
Under 1 year	45
1– 2 years	65
2– 4 years	57
4– 8 years	51
8–12 years	41
12–16 years	34
Over 16 years	32

In 8 instances, tests were made on both infants and their mothers. In five cases the mother and the child showed the same reaction to the test; in 1 case the mother had a positive reaction and her baby a negative one; in 2 cases the mothers had negative reactions and the babies positive ones. In 1 instance a wetnurse had a negative reaction and her foster baby a positive one.

Of the girls, forty-seven per cent showed a positive reaction, while of the boys only 36 per cent had a positive reaction.

In children with acute illnesses, such as measles, pertussis and scarlet fever, the percentage with a positive reaction seems higher than in controls. Children with postdiphtheritic paralaysis who had not received antitoxin usually had a positive reaction to the Schick test.

HIGGINS, Boston.

REACTION WITH INACTIVATED TOXIN AS COMPARED WITH THE SCHICK TEST IN A STUDY OF THOSE SUSCEPTIBLE TO DIPHTHERIA. V. PINTOZZI, Riv. di clin. pediat. **30**:1340 (Oct.) 1932.

Heat was used to inactivate the diphtheria toxin. Comparative tests with the inactivated toxin and with the toxin as used in the Schick test were made on 1,605

children. Positive reactions with the inactivated toxin (pseudoreactions) occurred in 200 of the patients, 49 of whom had positive reactions to the Schick tests and 151 of whom had negative reactions to the Schick tests. The pseudoreactions occurred in approximately 13 per cent of children of all age groups, except in babies under 1 year, none of whom showed a positive pseudoreaction; positive reactions occurred in 23 per cent of adults.

The pseudoreaction, which is presumably due to protein in the broth in which the toxin was made, is apparent in twenty-four hours; it has entirely disappeared in seventy-two hours, at which time the Schick test is usually read.

HIGGINS, Boston.

CAPILLARY TEST IN THE CHILD WITH PARTICULAR REFERENCE TO CAPILLARY RESISTANCE IN MEASLES. ENRIQUE JASO, Pediatria españ. **21**:396 (Mayo) 1932.

Capillary resistance is diminished in measles. The value varies between 5 and 10 cm. of mercury. About the fifth day after the beginning of the exanthem, the pathologic fragility begins to recede, with values above the normal during convalescence. The author believes that this change in some way is connected with the development of immune reactions.

The capillary fragility is not confined to the affected portions of the skin alone, but is also present in the sound skin not affected by the exanthem.

The Rumpel-Leeds phenomenon is always positive.

SCHLUTZ, Chicago.

TREATMENT OF DIPHTHERIA. LUIS M. ZUVIRÍA, Rev. méd. latino-am. **17**:1581 (Aug.) 1932.

The author discusses the possible benefits of using the bacterioserum of Lemos. This serum contains a mixture of antitoxin and bacteria, the theory being that a passive immunity is formed. The usual dosage of this preparation is 10,000 units.

SANFORD, Chicago.

RETURN CASES OF SCARLET FEVER. W. KNOEPFELMACHER, Arch. f. Kinderh. **95**:246 (Feb. 5) 1932.

The occurrence of scarlet fever among persons in contact with patients with scarlet fever discharged from the Carolinen Kinderspital has been studied for a number of years. For the three years previous to 1924, the percentage of such return cases was from 5 to 10. Since that time, with the use of cubicles and smaller rooms and the keeping of the children on an open air veranda for one week before dismissal, the percentage has fallen to 1.8. The mothers are also advised to keep the child in the country away from other children for a period of two weeks. The stay in the hospital is usually six weeks. Other factors which may have influenced the number of return cases is the mildness of recent epidemics, improvements in hygiene and a decrease in the size of families.

LESLIE, Evanston, Ill.

SCARLET FEVER IN ISOLATED INSTITUTIONS. ERNST SLAWIK, Arch. f. Kinderh. **95**:261 (Feb. 5) 1932.

Reports are given and the measures taken for the prevention of spread of the epidemics and the bacteriologic findings are discussed. The adult attendants were given passive immunization as a temporary measure. No direct relationship was found between ordinary sore throat and scarlet fever; the incidence of the former was not greater than at other times, and in several who had recovered from an attack of sore throat, typical cases of scarlet fever later developed. The Dick test was not used.

LESLIE, Evanston, Ill.

NONSPECIFIC VAGINAL DISCHARGE IN CHILDREN. KURT PAUL, Arch. f. Kinderh. **97**:63 (July 22) 1932.

In more than half of 135 cases of nongonorrheal vaginitis in children pseudodiphtheria bacilli were found. They could not be differentiated morphologically or culturally from true diphtheria bacilli, but were not pathogenic for guinea-pigs. In almost one fourth of the cases the increased discharge was due to the physiologic changes of prepuberty, in which the vaginal secretion becomes more acid and bacilli become predominant. The remaining cases were due to B. coli, staphylococcus, streptococci and other organisms.

LEMASTER, Evanston, Ill.

VACCINATION AGAINST SMALLPOX IN INFANTS. MARIA J. VAN STOCKUM, Kinderärztl. Praxis **3**:8 (Jan.) 1932.

The author reports observations made on a large number of Javanese infants vaccinated during the first year of life. Aside from fever, the most frequent complications were diarrhea, bronchitis, otitis media, eczema, pyodermia, conjunctivitis and lymphadenitis subaxillaris. In cases in which there were no complications, anorexia frequently occurred, accompanied by a lowered rate of gain in weight. A lowered immunity to infection was definitely manifested by infectious sequelae which could be definitely traced to the vaccination. In infants vaccinated in the first three months of life there was less tendency toward complications than in those vaccinated later.

HUENEKENS, Minneapolis.

PEDIATRIC LITERATURE OF SOVIET RUSSIA (1929-1931). S. J. SCHAFERSTEIN, Kinderärztl. Praxis **3**:87 (Feb.) 1932.

The Russian pediatricians are chiefly concerned with scarlet fever, diphtheria, pertussis and epidemic meningitis.

HUENEKENS, Minneapolis.

DIPHTHERIA BACILLI IN THE SECRETIONS OF THE EAR. HERMINE PREIDT, Ztschr. f. Kinderh. **53**:304, 1932.

In twenty cases of otitis, diphtheria bacilli were isolated from the ears in 28 per cent of the cases. In spite of the virulence of the organisms, as determined by inoculation into animals, diphtheritic complications were absent in all the cases. The relation of these findings to the epidemiology of diphtheria is discussed.

SHELLING, Baltimore.

THERAPEUTIC EFFECT OF FRESH PERTUSSIS VACCINE. M. TOKUNAGA, J. Pediat. (Tokyo), July 20, 1932, no. 386, p. 1249.

The author prepared a fresh pertussis vaccine by culturing in three successive generations the organism obtained from the sputum of the patient. The final product contained 2 mg. of the organism in 1 cc. of physiologic solution of sodium chloride, heated and preserved with 0.5 per cent phenol. The preparation was used as an autogenous vaccine in five cases and as a general vaccine in ten cases, but the therapeutic effect was the same in both groups. The course of the disease was about two weeks in cases in which this vaccine was used. The author fails, however, to give the results in control cases to prove his point.

KATO, Chicago.

BLOOD SUGAR AND RESIDUAL NITROGEN IN TYPHOID FEVER IN CHILDHOOD. F. MATSUDA, J. Pediat. (Tokyo), July 20, 1932, no. 386, p. 1270.

The author, using Bang's micromethod, made a series of quantitative determinations of the blood sugar and residual nitrogen in forty-seven cases of typhoid fever observed in the pediatric service of Nagasaki Medical College. He found that the blood sugar showed a decided increase during the febrile period, just as in

the adult, and a definite decrease during the afebrile period. He also noted a relation between the severity of the disease and the amount of hyperglycemia. The blood sugar was also elevated in the presence of complications, particularly dysentery, pneumonia and nephritis. There were no significant abnormalities or characteristics in values for residual nitrogen in these patients. KATO, Chicago.

TONSILS AND RHEUMATISM. H. BURGER, Nederl. tijdschr. v. geneesk. **76**:1451 (March 26) 1932.

In this clinical lecture, the origin of angina in relation to the functions and the significance of angina in several conditions are discussed. The author reports cases illustrating alleviation or quick cure of a rheumatic condition of long duration by tonsillectomy; however, this effect could not be verified by statistics. Other measures than tonsillectomy have no value. Frequently occurring attacks of angina are also an indication for tonsillectomy in the period between two attacks. In every case of angina, with an infectious complication, tonsillectomy must be considered. Rheumatic conditions that began with an attack of angina are often not of too long standing for tonsillectomy to be performed with the desired result. The coexistence of rheumatic conditions together with chronic tonsillitis is an absolute indication for tonsillectomy. The presence of enlarged lymph glands behind the angulus mandibulae verifies a doubtful diagnosis. Tonsillectomy performed by a skilled surgeon is almost free from danger. In two thousand tonsillectomies, only two patients died (in one death was due to the narcosis and in the other, to status thymicolymphaticus). Severe hemorrhages were not seen. Only once was the bleeding so severe that a second operation had to be performed.

VAN CREVELD, Amsterdam, Holland.

FOOD POISONING IN MEN IN RELATION TO PIGEON PARATYPHOSIS. A. CLARENBURG and C. G. J. DORNISKX, Nederl. tijdschr. v. geneesk. **76**:1579 (April 2) 1932.

Twenty persons were afflicted with gastro-enteritis after having consumed pudding of which the most important ingredient was pigeon eggs. In the pudding were found paratyphus bacilli of the Aertrycke type. The same kind of microorganism was discovered in the feces, the blood and the urine of the patients. Examination of the blood serum of the patients also revealed the presence of agglutinins for these bacteria. Among the pigeons from which the eggs were procured cases of paratyphus were found. It was demonstrated that the paratyphus bacilli in the eggs of these birds were identical with those in the cultures obtained from the pudding and the patients. The food poisoning was caused by infection of the pudding with paratyphus bacilli from the pigeon eggs. This is the first case demonstrating that the paratyphus bacilli of pigeons can be harmful to man.

VAN CREVELD, Amsterdam, Holland.

SCARLATINA PROTRAHENS. L. WENTINK, Nederl. tijdschr. v. geneesk. **76**:1710 (April 9) 1932.

A case of scarlet fever in a boy of 3 years had a remarkable course. There were three attacks of the condition, the one following the other immediately, during five weeks. The first attack was very light, the second, light and the third, serious but not fatal. There were no complications.

VAN CREVELD, Amsterdam, Holland.

TRANSVERSE LINES ON ROENTGENOGRAMS OF THE LONG BONES IN CHILDREN. M. DE BRUIN, Nederl. tijdschr. v. geneesk. **76**:2096 (April 30) 1932.

Roentgenograms of the long bones of normal children up to the age of 14 years often show one or more transverse lines at the end of the diaphysis. A

description of these lines is given, and the differential diagnosis with regard to other transverse shadows is discussed. These lines are caused by anatomic changes in the long bones, which occur when the normal growth is hampered or stopped. The retardation of growth results from starvation or various diseases. Therefore, these lines are called growth lines, or, better, growth-retardation lines.

VAN CREVELD, Amsterdam, Holland.

THE DOSE OF QUININE IN MALARIA. A. LICHTENSTEIN, Nederl. tijdschr. v. geneesk. **76**:3143 (June 25) 1932.

From an extensive comparative examination it appeared that the malaria parasites in Malang (Dutch Indies) die as quickly from 0.6 Gm. of quinine hydrochloride as from a dose of 1.2 Gm. of quinine; also that the symptoms of the disease disappear with equal rapidity. The following explanation is given: The human body possesses a certain quantity of antibodies, often sufficient to conquer a slight attack of malaria. Quinine partly destroys the malarial parasites, so that antigens are set free which may stimulate the formation of immune substances. These immune substances are able to destroy malarial parasites, with the effect that new antigens are set free which stimulate the formation of immune substances. In order to start this process a relatively small optimum dose of quinine is necessary.

In malaria perniciosa one has to deal with very resistant malarial parasites, so the formation of antigen is very slow; the immune substances also appear very slowly in the circulation, so that it takes a longer time to overcome an attack.

Experience teaches that 30 mg. of plasmochin in sufficient to kill the gametes, and the author recommends a dose of 0.6 mg. of quinine hydrochloride and 30 mg. of plasmochin as the basis for the treatment of malaria.

VAN CREVELD, Amsterdam, Holland.

PARATYPHUS IN CHILDHOOD. E. GORTER, Nederl. tijdschr. v. geneesk. **76**:3922 (Aug. 13) 1932.

In this lecture the different clinical courses which paratyphoid infection in children may take are illustrated by the description of several cases.

VAN CREVELD, Amsterdam, Holland.

Chronic Infections

SYPHILIS OF THE FETUS AND NEWBORN INFANT. FRED L. ADAIR, Am. J. Obst. & Gynec. **23**:111 (Jan.) 1932.

Syphilis is still a frequent cause of morbidity and mortality among fetuses and infants. It can be successfully treated only prior to birth. If the condition could be treated in the parents prior to conception or in the mother during pregnancy, the occurrence in the fetus and the new-born could be practically eliminated. The eradication of this contagious disease is a problem common to all localities and all countries. The transmission of the disease is now generally accepted as being maternal. The effect on the fetus depends on the virulence of the infection and the resistance of the mother. The older the disease in the mother the less the effect on the fetus. The more adequate the treatment in the mother the less the risk to the fetus. It is difficult to know whether the toxins may affect the fetus without an actual invasion of the fetus by the spirochete.

In a series of over 1,000 autopsies performed on fetuses and newly born infants at the University of Minnesota Hospital there were about 46 syphilitic infants (4.4 per cent). This series included only stillborn and newly born infants. The Wassermann test in the mother was positive in 28 cases, not made in 6 and negative in 12. In the entire series there were 501 stillbirths, of which 7.4 per cent were syphilitic. In the group of 46 syphilitic infants, 36, or 78.2 per cent,

were prematurely born and 10, or 21.7 per cent, were full term. Spirochetes were found in the fetal tissues of 41. Osteochondritis syphilitica was present in 37. Splenomegaly was present in 35; hypertrophy of the liver, in 25; gumma of the liver, in 3; pneumonia alba, in 8; pancreatitis, in 11, and characteristic changes of the skin.

ZIEGLER, Minneapolis.

VALUE OF ROENTGENOGRAPHY IN THE DIAGNOSIS OF CONGENITAL SYPHILIS: INFANTS CONSIDERED. EDWARD C. VOGT, Am. J. Roentgenol. **26**:96 (July) 1931.

In this study are presented the complete clinical and roentgenologic records for 109 children under 2 years, in whom a diagnosis of congenital syphilis was considered proved. A positive Wassermann test of the blood was found in 91.2 per cent, and a positive Wassermann test of the spinal fluid was found in 16 per cent of the 38 cases in which this test was made. The roentgen findings are classified as: (*a*) production of bone as subperiosteal thickening; (*b*) destruction of bone, or osteomyelitis, and (*c*) disturbance of growth. Subperiosteal thickening was the most frequent finding, being present in 78 per cent of the cases. The periostitis should be bilateral and involve multiple bones. It is often associated with (*b*) and (*c*). Dactylitis was present in 16 per cent of the cases, and in one case it was the only lesion noted. Osteomyelitis, as evidenced by the absorption of bone and usually accompanied by the formation of new bone, was shown in 63 per cent of the cases. It is found most often at or near the ends of the long bones and may involve the epiphyses, but since cartilage is not opaque, one cannot discover from the roentgenograms just when this process occurs. For this reason, the word osteochondritis is purposely omitted. Osteomyelitis, appearing as bilateral semilunar defects at the upper ends of the tibiae medially, and adjacent to, or just below, the epiphyseal line appeared in 45 per cent of the cases of this series, and is considered pathognomonic of syphilis. Disturbance of growth may be demonstrated as a dense narrow line at the ends of the diaphyses, but as such is not diagnostic of syphilis. However, when the dense line is present in cases of syphilis, a parallel zone of diminished density, just proximal, will be shown frequently, which is very suggestive. When the metaphyseal margins are serrated the findings are very characteristic. Of 27 roentgenograms of skulls, 7 revealed irregular destruction or slight thickening of the cranial vault, which was evidently of syphilitic origin. A common location for erosion of the skull is along the lambdoid and posterior portion of the sagittal, with the result that a wide gap occurs in which there are multiple small bony spicules. Two patients showed separation of all the sutures in no way different from that in nonsyphilitic hydrocephalus. All of the patients under 1 year of age who had involvement of the skull also showed diagnostic evidence of syphilis in the bones of the extremities; in 18 cases repeated examinations were made following the institution of antisyphilitic treatment and all showed progressive healing.

STULIK, Chicago.

ROENTGENOLOGIC ASPECTS OF CHILDHOOD TUBERCULOSIS. BENJAMIN GOLDBERG, Am. J. Roentgenol. **26**:397 (Sept.) 1931.

The term "childhood type of tuberculosis" was defined by the American Sanatorium Association, in May, 1929, to describe the diffuse or focal lesions in the lungs and adjacent tracheobronchial nodes that result from the first infection of the pulmonary tissue with the tubercle bacillus. It has no essential reference to age, but merely defines the type of tuberculosis resulting from a primary infection of the lungs. The primary pulmonary focus, as originally described by Kuss and Ghon, and the secondary changes in the bronchopulmonary, tracheobronchial and paratracheal glands constitute the "primary complex" pathognomonic of the disease. Besides the actual physical findings, the problem of diagnosis involves an accurate history of possible contact, the symptom complex, laboratory

tests and roentgen study. A careful analysis of hilar shadows involves a knowledge of the anatomy and physiology of the pleura, the bronchi, the glands and the lymphatics. A knowledge of pathology and pathologic sequence is also important in the interpretation of the shadows. A discussion of the pathogenesis and pathologic sequence of the primary focus, secondary glandular involvement, miliary tuberculosis, epituberculosis, secondary diffuse parenchymal lesions and apical tuberculosis is accompanied by a series of roentgenograms, which illustrate the details. The apical type of tuberculosis is not childhood tuberculosis, but is an adult type occasionally seen in children.

STULIK, Chicago.

THE BEHAVIOR OF THE MONOCYTES IN TUBERCULOSIS IN CHILDREN. WILLIAM ANTHONY REILLY, Am. Rev. Tuberc. **25**:179 (Feb.) 1932.

The monocyte count and ratio give valuable evidence in most cases of tuberculosis of the hilar lymph nodes. Observations made in thirty-two tuberculous and five nontuberculous girls indicate that in active tuberculosis the monocytes increase in number and the lymphocytes decrease, while the reverse holds true when inactivity sets in. The patients in the aforementioned group had mainly lesions of the hilar nodes. In clinically active tuberculosis the observations on the blood corroborated the clinical impression of activity in 62.5 per cent of the patients.

The ratio of monocytes to lymphocytes corroborated the impression of clinical activity in 92.3 per cent of the patients, while the actual number of cells corroborated the impression in only 76.9 per cent.

SMITH, Ogden, Utah.

A COMPARATIVE STUDY OF THE PIRQUET AND MANTOUX TUBERCULIN TESTS IN SCHOOL CHILDREN. S. A. SLATER and KATHLEEN JORDAN, Am. Rev. Tuberc. **25**:218 (Feb.) 1932.

The authors have endeavored to make a comparative study of the two tests under similar conditions, and to determine, if possible, which test is the most practical in the fight against tuberculosis, rather than which gives the highest percentage of reactors. Their work did not reveal the existence of such great differences as most writers maintain. Their figures are: Mantoux, 10.4 per cent and Pirquet, 9.15 per cent. The two tests were made on 1,004 children. The greatest difference was shown in connection with the ages of those reacting to the two tests. The average age of those reacting to the Mantoux alone was 14 years and of those reacting to the Pirquet test alone, 10.6 years. Possible explanations are that the Mantoux test, being more sensitive, elicits reactions in the older children who have had casual contact or a slight infection. Also the older child may have overcome the old infection and reacts only to the more sensitive test. It may also be that the more tender skin of the younger child is more sensitive to the Pirquet test. It would appear from the study as a whole, that neither test is infallible, and that for the sake of accuracy, both tests should be used or the Mantoux test repeated, with a larger dosage. On the other hand, this study indicates that when subjects are infected at home, they are most likely to react to the Pirquet test, which therefore seems to be a more practical method of determining the source of infection.

SMITH, Ogden, Utah.

THE INCIDENCE OF TUBERCULOUS INFECTION AMONG STUDENTS OF A HIGH SCHOOL. EDITH S. HEWITT and ROLLIN E. CUTTS, Am. Rev. Tuberc. **25**:525 (April) 1932.

Of 1,328 high school students in Rochester, Minn., 11.5 per cent gave positive reactions to the Mantoux test. Of 34 students definitely known to have been exposed to open tuberculosis, 61.8 per cent gave positive reactions. The lesions disclosed roentgenologically were few in number and not extensive. No case of active or extensive latent tuberculosis was found.

SMITH, Ogden, Utah.

COMPARATIVE VALUE OF PIRQUET AND MANTOUX TESTS IN COLORED INFANTS AND CHILDREN. MORRIS GLEICH, Arch. Pediat. **49**:399 (June) 1932.

Basing his conclusions on two hundred cases, the writer objects to the statement that a Mantoux test is the only reliable test and that the Pirquet test should be discontinued. He feels that the Pirquet test should be employed first, especially among the Negroes, French, Viennese and Porto Ricans, in whom the incidence of tuberculosis is high.

WADDELL, University, Va.

THE SCHICK TEST IN INFANCY. JOSEPH GREENGARD, Arch. Pediat. **49**:526 (Aug.) 1932.

In a group of 584 infants, periodic Schick tests were made. The curve of incidence of positive reactions according to age groups is found to be in strict agreement with the present knowledge on this subject. The transition from a negative to a positive reaction was demonstrated in 114 infants.

Comparative Schick tests were carried out on a group of 100 mothers and their newly born infants. In this group a definite lack of agreement between the reactions of the newly born infants and those of their mothers was demonstrated. Sixty per cent of the newly born infants whose mothers had a positive reaction gave negative reactions to the Schick test, and in every instance in which a positive reaction was obtained in both the infant and the mother, the reaction of the infant was much less strong than that of the mother. All the infants of mothers whose reaction was negative reacted negatively. The incidence of the positive Schick test in infancy varies from 17.6 in the new-born period to 70 per cent at 1 year of age. About 80 per cent of the infants were found to have lost their immunity by the end of the ninth month. The writer believes that a positive Schick test is indicative of a lack of specific immunity in the newly born infant, and that a negative Schick test is of no significance in the newly born infant, since a large proportion of infants without immunity to the antitoxin show no reaction to intradermal toxin.

WADDELL, University, Va.

TUBERCULOUS MENINGITIS IN CHILDREN. PHILIP ROSENBLUM and M. I. MAKLER, Arch. Pediat. **49**:667 (Oct.) 1932.

A study of 101 cases of tuberculous meningitis occurring over a period of eighteen months is presented. The writers review present knowledge as to incidence, etiology, symptoms and signs, pathology, diagnosis and treatment.

WADDELL, University, Va.

TUBERCULOSIS IN CHILDREN. LEE FORREST HILL, J. Pediat. **1**:504 (Oct.) 1932.

The general subject of tuberculosis in children is discussed with numerous references to the literature. The general characteristics of the childhood type of tuberculosis are as follows: (1) Common in children, rare in adults; (2) results from first infection; (3) associated tracheobronchial lymph nodes always involved, not always demonstrable; (4) no preferred sites in the lungs; (5) caseous lesions followed by calcification and slight fibrosis; (6) infiltrated areas resolve, leaving little or no scars; (7) greater tendency to rapid spread and development of miliary tuberculosis.

In making a diagnosis of tuberculosis in children, chief dependence must be placed on the history of exposure, the tuberculin reaction and the roentgenologic studies. Several reports showing a variable incidence of tuberculosis in children in various localities are discussed.

In general, the prognosis of tuberculosis in childhood is much better than was previously considered. However, the adult type of tuberculosis in children in their teens carries a grave outlook. During the active stage of tuberculosis the mono-

cytes of the blood are increased, while the lymphocyte count is decreased. Of course, tuberculosis is much more frequent in children exposed in their own home. It is suggested that further work with the B C G vaccine is needed before its value and safety can be accepted.

LEMASTER, Evanston, Ill.

THE CHILDHOOD TYPE OF TUBERCULOSIS. J. B. MCKNIGHT, Texas State J. Med. **28**:263 (Aug.) 1932.

In this study the tuberculous infections of children have been divided into: 1. The adult or pulmonary type of tuberculosis, which is the more serious form. The severe condition is usually caused by delayed diagnosis or negligence in the proper care of the child having the childhood type of the disease. 2. The childhood form of tuberculosis or primary complex. This is the milder and initial form which the disease appears to assume in children. The prognosis is directly in proportion to the patient's ability to wall off the infection and to prevent its spread to the other parts of the lung.

The author points out that in many cases the condition is recognized very late, and that because of its frequency, tuberculosis should be considered in every case in which it is difficult to make a positive diagnosis. The diagnosis depends on a careful and thorough consideration of all of the following factors: (1) A detailed history, including an investigation of the familial association factors. 2. Symptoms and physical signs, including a comparison of activities with those of normal children. One is justified in directly comparing the lack of gain in weight in children to the loss of weight in an adult. Coughs, nervousness, elevations in temperature and pain are more frequent findings than hemoptysis and the demonstrable presence of the tubercle bacilli in the sputum. 3. The results of the Mantoux or the intracutaneous tuberculin test, which is the most sensitive, most dependable and the most efficient test. 4. Roentgen examination, which is a valuable clinical support when interpreted by an experienced roentgenologist.

It is to be urged that all of the diagnostic aids should be used collectively in order that a definite dependable diagnosis may be ascertained.

MOORE, Dallas, Tex.

THE PREVENTION OF TUBERCULOSIS IN CHILDREN. E. A. WRIGHT, Texas State J. Med. **28**:266 (Aug.) 1932.

The results of a tuberculin test in two thousand school children in Houston, Texas, made by the author, show a positive reaction in an average of about 17 per cent. The Mantoux test was used. The country schools showed a higher per centage of positive reactions than the city schools. The laboratory observations in each case were accompanied by a thorough physical examination, a complete history, and roentgen, serologic, urologic and sputum studies.

This report represents a program in Houston, Texas, that has barely begun. It might be stressed that the reaction of the skin only forms a basis on which diagnosis and prognosis can be determined. Prevention of tuberculosis may be accomplished when prevention of contact is successfully instituted. This can be done only by isolation of patients with open tuberculosis and a close follow-up of patients with closed tuberculosis.

MOORE, Dallas, Texas.

VACCINATION AGAINST TUBERCULOSIS WITH B C G: THE PRESENT STATE OF THE QUESTION. A. CALMETTE, Brit. J. Tuberc. **26**:115 (July) 1932.

On the basis of reports to the Pasteur Institute from forty-six distinguished clinicians, bacteriologists and veterinary surgeons working in the principal nations of the world, Calmette reasserts his convictions as to the value and the innocuousness of vaccination with B C G. It is a living virus comparable to cowpox. Its attenuation is hereditarily fixed, as is the case with Jenner's vaccine and Pasteur's

vaccines against anthrax and hydrophobia. It possesses definite antigenic properties and gives rise to tuberculin allergy. No valid evidence has been offered to indicate an eventful return of virulence in the human organism. The author emphatically states that during ten years of vaccination with B C G, not a single accident has been observed that could rightfully be attributed to this agent. Infants who have absorbed B C G during the first ten days of life not only resist all family contagion, but probably acquire a paraspecific immunity as well. It has been noted everywhere that vaccinated children are less likely to have the ordinary diseases of childhood than are nonvaccinated children living under the same conditions. Figures compiled by expert statisticians in Sweden, Holland, Poland and Rumania and elsewhere, summarizing the results of observations of vaccination with B C G in 443,656 children, indicate that the average mortality from all causes from birth to the age of 1 year has been: (1) for vaccinated children, 7.9 per cent, and (2) for nonvaccinated children, 15.3 per cent. Practically the same figures obtain in France where more than 450,000 children have been vaccinated since 1924.

SMITH, Ogden, Utah.

TUBERCULOSIS INFECTION IN INFANCY AND CHILDHOOD. DAVID R. HAMILTON, Brit. J. Tuberc. **26**:118 (July) 1932.

Hamilton's observations were made on 1,092 children in an industrially depressed area. Tuberculous infection was determined by the Pirquet test, with recourse to the intradermal test in borderline reactions. At the age of 2 years, one child in every ten was found to be infected, and at the age of 3, the ratio was one in three. Aside from a progressive increase in incidence of infection with increasing age, he found a sharp increase between the ages of 2 and 4. In explanation it is suggested that this is the "dirty" age, when children are essentially "ground animals," crawling about floors and pavements with greater chances of contact with infectious material. The value of the test in diagnosis decreases with increasing years except that in older children negative tests are of value in excluding tuberculous disease. The incidence of extrafamilial infection was found to be as high as 50 per cent, so that in any hypothetic family of ten children under 15 years, five may be presumed to have become infected from such source. In a similar family, if the father's sputum gives a positive reaction, the number of infected children will be six. If the patient with open tuberculosis is the mother, eight of the children are infected. If the patient is a brother or a sister, nine are infected. The influence of malnutrition is not easy to assess, but in this study two facts emerge: In the first five years of life, good health is a more frequent concomitant of latent tuberculosis than is malnutrition. The incidence of malnutrition decreases with age while that of infection increases. However, in undernourished children who have come in contact with tuberculosis, the frequency of infection is much higher than in the normal children who come in contact with the disease, and the more severe the degree of malnutrition the greater is the likelihood of infection.

SMITH, Ogden, Utah.

THE PRESENCE OF THE TUBERCLE BACILLUS IN MILK. S. ROODHOUSE GLOYNE, Tubercle **13**:443 (July); 488 (Aug.) 1932.

There appears to have been little if any reduction, in England, in the contamination of milk by the tubercle bacillus during the past twenty years. Two methods of examination have been used for many years: (1) examination of the direct film of centrifugated deposit, and (2) inoculation of guinea-pigs. The first is almost valueless in the case of bulked samples, but may be of value in samples from a single cow. For bulked samples, the guinea-pig test is essential, although it is not infallible. In addition to these older methods, there has been introduced a cultural test, the value of which is at the moment difficult to assess.

SMITH, Ogden, Utah.

SYPHILITIC PERITONITIS. H. SLOBOSIANO, Nourrisson **20**:286 (Sept.) 1932.

Three cases of syphilitic peritonitis were observed in six thousand deliveries. The peritonitis was accompanied by lesions in the intestines, liver and spleen. All three infants were stillborn.

McCLELLAND, Cleveland.

THE ULTRAVIRUS OF TUBERCULOSIS. B. ROSENKRANZ, Rev. franç. de pédiat. **7**: 369 (Oct.) 1932.

The author presents an excellent review of this subject, with a complete bibliography.

SANFORD, Chicago.

INTERMITTENT PERIPHERAL CYANOSIS AND HYPERTROPHY OF THE THYMUS IN A SYPHILITIC INFANT. F. MANNARINI, Prat. pediat. **10**:249 (June) 1932.

The author carefully describes the case of a baby who had been having attacks of coughing, dyspnea and peripheral cyanosis, which were first noticed during the third week of life. At 4 months, it was found to have an enlarged thymus as evidenced by physical and roentgen examination. During two months of roentgen treatment, the thymus decreased in size and the attacks became not only less severe but less frequent. The diagnosis of syphilis was made on the basis of the positive results of serologic examination of the parents. The major portion of the paper is devoted to an excellent discussion of the differential diagnosis of the various types of congenital heart disease in particular relationship to this case.

DOOLEY, Kent, Conn.

MODE OF ACTION OF THE GERSON-HERRMANNSDORFER-SAUERBRUCH REGIMEN IN THE TREATMENT OF TUBERCULOUS INFECTIONS. R. PACHIOLI and G. GIANNI, Riv. di clin. pediat. **30**:664 (May) 1932.

The Gerson-Herrmannsdorfer-Sauerbruch regimen is mainly dietary; there is a diet low in sodium chloride, high in vitamins, high in vegetable protein and high in fat; cod liver oil with phosphorus and a preparation rich in calcium salts are given.

In seven tuberculous children given this diet, the alkali reserve of the blood serum was slightly increased (an average of 52 mg. before and of 56 mg. afterward); but the p_H was essentially unchanged. The sodium chloride of the blood was diminished (496 mg. per hundred cubic centimeters before and 469 mg. afterward). The calcium content of the blood was essentially unaffected by the diet.

The Gerson-Herrmannsdorfer-Sauerbruch regimen is more successful in the treatment of tuberculosis of the skin than in pulmonary tuberculosis. Perhaps the withdrawal of sodium chloride from the skin may be the explanation of this clinical observation.

HIGGINS, Boston.

Internal Diseases

ROENTGENOLOGICALLY DEMONSTRABLE CHANGES IN BONE IN GAUCHER'S DISEASE. B. R. KIRKLIN and HANS W. HEFKE, Am. J. Roentgenol. **24**:258 (Sept.) 1930.

According to Junghagen, the bone changes in Gaucher's disease may be: (1) marked general osteoporosis; (2) porous and trabeculated spongiosa; (3) destruction of the spongiosa, either in small or in large areas; (4) thinning of the cortex and widening of the long bones, particularly the lower end of the femur, and (5) compression of diseased bones, particularly the head of the femur by the weight of the body. The authors' patient, a woman, aged 26, two years after splenectomy, revealed enlargement of the medulla and thinning of the cortex in the

humerus and radius of both arms and of the upper ends of both femurs. The thorax, spine, pelvis and skull were normal in spite of a gain of 10 pounds (4.5 Kg.). The changes resembled those in marked senile atrophy.

STULIK, Chicago.

CAMPIODOL (IODIZED RAPESEED OIL); ITS USE IN THE VISUALIZATION OF THE BODY CAVITIES. MARK ALBERT GLASER, Am. J. Roentgenol. **24**:477 (Nov.) 1930.

The author discusses the history and experimental studies of opaque material. Because of nonmiscibility, special products of iodized rape-seed oil were synthesized for various body cavities. The author's conclusions follow: 1. Iodized rape-seed oil is a stable, nontoxic oil containing approximately 43 per cent elemental iodine. 2. Straight iodized oil is satisfactory for the outlining of the tracheobronchial tree. 3. A 4:1 dilution with ethyl olive oil is satisfactory for outlining the spinal subarachnoid space, the cerebral and peripheral blood vessels, the female genitalia, the lacrimal ducts, the mastoids and the eustachian tubes. 4. A 50 per cent dilution with ethyl olive oil is satisfactory for outlining the nasal sinuses. 5. Emulsified iodized rape-seed oil is an inert, nonirritating substance, and has been successfully used in urography, with a minimum of irritative symptoms.

Ethyl olive oil is made by the reflux of a mixture of olive oil, absolute alcohol and concentrated sulphuric acid for four hours. The alcohol solution of ethyl esters formed is washed with ten volumes of water. The esters are dried, after separation, with anhydrous sodium sulphate. Remnants of ethyl alcohol are distilled off. The oil in this way is then further purified by distillation in vacuo (65 mm.) at temperatures ranging from 190 to 225 C.

STULIK, Chicago.

HYPERPLASIA OF THE THYMUS; A STUDY OF ONE THOUSAND AND FORTY-FIVE PATIENTS, INCLUDING AVAILABLE FAMILY AND MATERNAL HISTORY. S. W. DONALDSON, Am. J. Roentgenol. **24**:523 (Nov.) 1930.

Enlargement of the thymus seems to belong to family groups, and the majority of children in these families exhibit this condition. Roentgen examination is indicated in all children when the history shows that previous children of that family had an enlarged thymus. Certain types of thymic enlargements do not decrease in size after irradiation, but the symptoms in these cases subside. There is only unconvincing evidence that there may be a relation between enlarged thymus in the offspring and enlarged thyroid in the mother (thyroid disturbance). The age or multiparity of the mother or the obesity of either parent has no bearing on thymic hyperplasia. While there is some evidence that larger babies are more apt to have enlargement of the thymus than smaller ones, this is not enough to limit examination to the large babies. Findings were slightly more frequent in the girls in this series, though enlargement of the thymus does not necessarily indicate that the child will show symptoms. Early diagnosis is of vital importance, and diagnosis and treatment of an enlarged thymus is a problem for the radiologist, who should decide on roentgen or radium therapy.

STULIK, Chicago.

A ROENTGEN SIGN OF PLUMBISM: THE LEAD LINE IN GROWING BONE. EDWARD C. VOGT, Am. J. Roentgenol. **24**:550 (Nov.) 1930.

Two girls, one aged 2 years and the other 7 months, with conditions diagnosed as lead poisoning, revealed a dense zone at the ends of the diaphyses. Four recorded cases of lead poisoning in which roentgenograms had been made in the hospital showed this same line at the ends of the long bones, but this sign had been passed over previously, as probably indicative of healed rickets. The lead line is more compact and is readily differentiated from that in florid, healing

rickets and scurvy because of the absence of the other classic findings. Chemical analysis reveals that the lead was deposited in inverse ratio to the calcium. The zones of greatest density on the roentgenograms contained less calcium, but four times as much lead as the cortex. Therefore, it seems evident that the opacity was due to lead.

STULIK, Chicago.

DWARFISM DUE TO DISORDERED EPIPHYSEAL DEVELOPMENT. HOWARD E. RUGGLES, Am. J. Roentgenol. **25**:91 (Jan.) 1931.

The characteristic findings are short stature (rarely over 1 meter in height), a large head, widely spaced eyes, a depressed root of the nose, a narrow, prominent sternum, kyphosis, flexed hips, hands that reach almost to the knees, genu valgum, loss of muscle power without atrophy, fine hair, coarse skin and unimpaired mentality. The condition is congenital, and appears at from 2 to 3. months of age. The laboratory findings are negative, and the basal metabolic rate is from +10 to +20 per cent. Characteristic plates reveal a profound disturbance of epiphyseal development, a normal calvarium, a small sella turcica, heavy ribs expanded at the costal cartilages and pointed metacarpal bases. Ossification begins in the distal row of carpal bones, the epiphyseal zones of the radius and ulna are rotated markedly toward each other, the heads of the femur are usually absent and the acetabula are eroded upward and are irregular in outline. There are relative shortening of the fibulae, irregularly outlined tarsal bones, pointed metatarsal bases, wide, flat, vertebral bodies, intervertebral disks as thick as the vertebrae and vertebrae of ragged outline. In the differential diagnosis achondroplasia is considered. Treatment with thyroid, pituitary and other extracts yields negative results. The determination of the etiology will depend on observations at autopsy.

STULIK, Chicago.

CONGENITAL IDIOPATHIC ENLARGEMENT OF THE HEART. GEORGE W. HOLMES, Am. J. Roentgenol. **25**:320 (March) 1931.

Enlargement of the heart in infancy and childhood, with no pathologic basis, is rare, but sudden death frequently follows any unusual strain on the heart in these cases, and both the symptoms and roentgen findings resemble closely those seen in enlarged thymus. In 1928 Stoloff found thirty-four cases in the literature, but considered only seventeen of these true idiopathic enlargement. In most of the reported cases the size of the heart is enormous; the average duration of life is fourteen months; frequently the terminal illness occurred at about the time the child began trying to walk or was preceded by an attack of pertussis. In several cases there was an associated enlargement of the thymus gland. Dyspnea, cyanosis or both were present at some time in almost every case. Physical examination usually revealed an enlarged heart, and at times a systolic murmur was heard. Bulging of the left thoracic wall seems to be a diagnostic sign of some value. The roentgenograms usually show a large cardiac silhouette, though at times it is difficult to distinguish the outline of the left upper border. Two case reports are presented. One of these was diagnosed ante mortem. The clinical and roentgen findings on which the presence of idiopathic enlargement should be suspected are: rapid breathing, with or without cyanosis, bulging of the thoracic wall over the cardiac area, enlargement of the heart to percussion and a soft systolic murmur heard at the apex.

STULIK, Chicago.

STUDIES IN STATUS LYMPHATICUS AND ITS RELATION TO ANESTHETIC DEATHS. W. N. KEMP, Anesth. & Analg. **11**:128 (May-June) 1932.

The author cites experimental, clinical and pathologic evidence to support the theory that status lymphaticus is caused primarily by the insufficiency of the

suprarenal cortex, with secondary hypertrophy of the thymus and lymph glands. He advises that an anteroposterior roentgen view of the chest be taken in suspected cases preoperatively.

LEMASTER, Evanston, Ill.

PEPTIC ULCER IN INFANTS UNDER ONE YEAR OF AGE. JEROME SELINGER, Ann. Surg. **96**:204 (Aug.) 1932.

Gastric and duodenal ulcers in infants under 1 year of age are not so rare as they were formerly supposed to be. Duodenal ulcer occurs more frequently than gastric ulcer.

The author presents statistics from large medical centers to show this incidence. At Bellevue Hospital in 7,700 autopsies, gastric ulcer was found in 5 children under 1 year of age. At the St. Louis Children's Hospital 5 cases of duodenal ulcer were found. Holt reports 4 cases in 1,800 postmortem examinations at the Babies' Hospital. Three cases of gastric ulcer in infants 2 months, 3 months and 11 months of age, respectively, are reported in detail.

Peptic ulcer is probably due to a combination of conditions. Any condition that lowers the general resistance predisposes to whatever the active agent may be. Some constitutional disease is usually the primary cause, with traumatism and infection the secondary causes.

Except in rare cases, the diagnosis is never made until perforation or persistent and massive hemorrhage occurs.

Treatment lies in early surgical intervention, but unless the diagnosis has been made early and operation resorted to before perforation or massive hemorrhage has taken place, the prognosis is poor.

BANTIN, Omaha.

CHRONIC MUCOUS GASTRITIS IN CHILDREN. CHARLES GILMORE KERLEY, Arch. Pediat. **49**:322 (May) 1932.

The author believes that this condition is quite frequent and should be suspected when the history of anorexia, regurgitation of food, eructation of gas, habitual vomiting and complaint of stomach pain, particularly when the stomach is empty, is obtained. Any or all of these symptoms may be present. The patient is usually underweight, and secondary anemia is not infrequent. Fatigue posture is rarely absent. By the elimination of possible disease agencies, such cases fall into the gastro-intestinal group. When a test normal breakfast is given, siphonage of the stomach five hours later, with lavage, reveals retained food and the presence of large quantities of thick tenacious mucus.

Three selected cases illustrating this condition are presented. The author reports good results by observing the following fundamentals in treatment: 1. There must be two free bowel evacuations a day. 2. The meal periods are invariably five hours apart. 3. The child is never coaxed or forced to eat. 4. Butter and cream are omitted from the diet, and skimmed milk only is employed at the commencement of treatment. 5. Orange juice before breakfast is omitted, and hot and cold drinks are avoided. 6. Abdominal support is supplied in the cases of ptosis, and postural defects are corrected. 7. Gastric lavage is performed, the frequency depending on the patient's response to treatment. 8. A warm bath is given at bedtime. 9. A rest plan is inaugurated; the patient remains in bed until 10 a. m., rests one and one-half hours after the midday meal and is put to bed, with lights out, at 7 p. m.

Parents are told that the child will lose weight the first week or two under the treatment and are asked not to weigh the patient. A dietary plan suitable for the age and condition is supplied. Breadstuffs, meats, poultry, fish, cereals, vegetables, skimmed milk, stewed fruits and puddings made from skimmed milk are given freely. Meats are best given in minced form for the younger patients. Cereal, such as oatmeal, cornmeal and whole wheat products, are cooked for four hours, and the coarser vegetables are put through a colander. Aromatic

extract of cascara sagrada is given in sufficient dosage three times daily to produce satisfactory elimination. In patients with redundant colon and sigmoid a Bassler belt is applied; mineral oil, one-half ounce (14.8 cc.) daily, is of service. The sphincter ani muscle is always examined and is stretched if found spastic.

WADDELL, JR., University, Va.

LAURENCE-MOON-BIEDL SYNDROME. WILLIAM ANTHONY REILLY and HANS LISSER, Endocrinology **16**:337 (July-Aug.) 1932.

In this paper, Reilly and Lisser give an excellent brief review of the literature regarding the Laurence-Moon-Biedl syndrome, with a table which presents in condensed form the essential features of each of the seventy-seven cases that have been recorded since Laurence and Moon reported the first one sixty-six years ago. This series includes four cases here reported for the first time.

The condition is characterized by dystrophia adiposogenitalis, atypical retinitis pigmentosa, mental deficiency, familial occurrence and skeletal abnormalities, most frequently polydactylism and syndactylism. There are a number of cases in which the classic syndrome is completely represented. A greater number of instances occur in which one or more of the characteristic symptoms are absent, but with familial occurrence as a *sine qua non* for the diagnosis.

The etiologic factors underlying this extraordinary malady remain obscure. The one autopsy yielded nothing characteristic. The hypophysis and the hypothalamus have been implicated by some writers, but the almost invariable familial occurrence demands consideration of peculiarities in the hereditary germ cells themselves.

The two typical cases reported in this paper occurred in sisters aged 11 and 13 years, respectively. The latter was obese, weighing 175 pounds (79 Kg.), and mentally retarded and had progressive dorsal kyphosis, which was first noticed when she was 10 years old, and progressive impairment of vision, which first attracted attention when she was 9 years old. There was external strabismus with nystagmus, and both retinas were partially detached and showed several areas of white exudate and many splotches of pigmentary infiltration.

The other sister had always been obese (weighing 117 pounds [53 Kg.] at 11 years of age) and had had queer, aimless motions of the body and limbs up to 3 years of age. Vision was impaired. There was a moderate kyphosis. Both eyes showed strabismus, nystagmus and atypical retinitis pigmentosa.

Both children have taken from 4 to 5 grains (0.26 to 0.32 Gm.) of thyroid extract and from 15 to 20 grains (0.97 to 1.3 Gm.) of whole pituitary extract daily for eight months. The older girl has lost 45 pounds (20 Kg.), is much more active and alert, and can see much better than before. The fundi show reattachment of the retina and resorption of old hemorrhage. The younger child has lost 20 pounds (9 Kg.) in weight and is much more alert, and the progressive failure of vision has stopped.

Two other probable, though atypical, cases are reported.

JACOBSEN, Buffalo.

THE OPHTHALMIC TEST FOR SENSITIVITY TO HORSE SERUM. L. N. CLAIBORN, J. A. M. A. **98**:1718 (May 14) 1932.

The definite need for a simple test which will give a more reliable index of the degree of susceptibility to horse serum led to a comparative study of the ophthalmic and intradermal tests. Of 465 patients, 5.6 per cent gave positive reactions to both tests, and 21.3 per cent to the intradermal test alone. All patients positive to ophthalmic tests were positive to intradermal tests. Undiluted serum was safely used for the ophthalmic test. The ophthalmic test was less sensitive, but gave a better clinical index of susceptibility than the intradermal test. Desensitization failed to alter the percentage of reactions.

BONAR, Salt Lake City.

RENAL CARBUNCLE IN INFANCY. M. F. CAMPBELL, J. A. M. A. **98**:1729 (May 14) 1932.

No record is available regarding the occurrence of renal carbuncle in infancy. The author reports two cases in 8 week old infants in which there was staphylococcic metastasis to the kidneys from cutaneous infections. The course and severity of the disease are similar to those in adults.

BONAR, Salt Lake City.

THE IDENTITY OF THE ALLERGICALLY ACTIVE SUBSTANCE IN THE GIANT AND LOW RAGWEED POLLEN. ARTHUR STULL, ROBERT A. COOKE and ROBERT CHOBOT, J. Allergy **3**:120 (Jan.) 1932.

Chemical and biologic data are given to show that the allergically active substance in the giant and low ragweed pollen is a water-soluble albuminous protein and is identical. Twelve cases of ragweed hay fever in which there was similar sensitivity of the skin were divided into two groups; six of the patients were treated with a routine extract containing the giant ragweed and six with an extract prepared from a low ragweed. All were equally well protected from hay fever.

HOYER, Cincinnati.

EMANATIONS OF FLIES AS EXCITING CAUSES OF ALLERGIC CORYZA AND ASTHMA. SALVATORE J. PARLATO, J. Allergy **3**:125 (Jan.) 1932.

Emanations from sand flies and the hairs and scales of moths and butterflies were found on glass slides placed in various places in the city and country. The emanations are found in the four summer months, and the amount on some days corresponded closely to the amount of pollen found on the slides. They are found, too, in house dust.

Four of the author's patients were sensitive to an extract of moths and butterflies.

This work was done nicely and showed the necessity of seeking out the causes of failure in the treatment of summer hay fever. HOYER, Cincinnati.

THE MECHANISM OF AN ASTHMATIC ATTACK IN CHRONIC ALLERGIC ASTHMA. BERNARD STEINBERG, J. Allergy **3**:139 (Jan.) 1932.

Injections of iodized rape-seed oil and roentgenograms were made in three cases representing a severe, a moderately severe and a mild allergic asthma. The injections were made and roentgenograms taken three hours after the attack in the patient with mild asthma of short duration, six hours after the attack in the moderately severe case and four days after the attack in the severe case. There is a lack of proper filling of the bronchial tree during a paroxysm, and this lack is proportionate to the severity of the attack of asthma and the frequency of previous paroxysms.

The observations were correlated with autopsy protocols found in the literature and with the author's own cases, and he assumes that the failure of the visualization of the bronchial tree is due to plugging with mucus from hyperfunctioning mucous glands. He believes that an asthmatic paroxysm is essentially due to this bronchial occlusion by mucus, and that bronchial constriction plays a part but is not responsible for the events preceding and following an attack.

HOYER, Cincinnati.

A STUDY OF THE APPARENT ATOPIC SIMILARITY OF CERTAIN CHENOPODIALES POLLENS. ERLE D. SELLERS and W. B. ADAMSON, J. Allergy **3**:166 (Jan.) 1932.

There is an apparent similarity of the atopens in the pollen of Amarantus spinosus, Amarantus palmeri, Amarantus retroflexus, and Acnida tamariscina,

but all the atopens of the aforementioned group are not contained in Salsola pestifer or Chenopodium album, although the latter are members of the same order of Chenopodiales.

"From this study it is suggested that only one of the members of the family Amaranthaceae studied need be used either in testing or in treatment of patients sensitive to any one or all of the six species studied."

These pollens are prevalent in the Southwest, especially Texas.

HOYER, Cincinnati.

MAXIMUM DOSAGE IN POLLEN THERAPY. GRAFTON TYLER BROWN, J. Allergy **3**:180 (Jan.) 1932.

Pollen extracts of varying strengths, up to 17.5 per cent, were tested on persons known to be sensitive. Reactions were proportionately greater as the strength of the extract increased above 1 per cent to 12.5 per cent, above which the degree of reaction was approximately the same. The nitrogen content of these extracts varied in the same way, being proportionately greater in the extracts until 12.5 per cent was reached; above this the strength of the nitrogen did not increase in proportion to the amount of pollen, there being but little difference between the 17.5 and the 20 per cent extract.

The author uses a 6 per cent and a 10 per cent extract of the pollens in treating his pollen-sensitive patients. He has three dilutions and the concentrated extract of each pollen so that he can give from 60 to 100,000 pollen units per cubic centimeter. The method of treating perennially is employed, and much larger doses are used than is customary. The treatment is continued until a negative reaction of the skin is obtained. A number of successful cases are reported in which the amount of extract used is given. The failure of other investigators with the perennial treatment of hay fever is believed, by the author, to be due to increasing the dose of the extract during the season. He does not increase his dose during the season, but continues with that dose which has been reached at the beginning of the season, and increases it again when the season is over.

HOYER, Cincinnati.

Nervous Diseases

MORTALITY AND EXPECTATION OF LIFE IN MENTAL DEFICIENCY IN MASSACHUSETTS: ANALYSIS OF THE FOURTEEN-YEAR PERIOD 1917-1930. NEIL A. DAYTON, CARL R. DOERING, MARGARET M. HILFERTY, HELEN C. MAHER and HELEN H. DOLAN, New England J. Med. **206**:555 (March 17); 616 (March 24) 1932.

As this splendid study covers about thirty pages and includes many interesting tables and graphs, it will be possible to abstract only the authors' summary, of about four pages.

This analysis was based on a study of 8,976 cases of mental deficiency with 878 deaths. These patients were admitted to, were in residence within or were discharged or died while in residence in, or on the books of, one of the three Massachusetts state schools between Jan. 1, 1917, and Dec. 31, 1930, inclusive. Specific death rates by age for each of three mental status groups, idiots, imbeciles and morons, are presented, these death rates being determined by the person-year method of constructing life tables.

The mortality among idiots is approximately 5 times that of the general population for both sexes. The mortality among imbecile males is 2.4 times that of the general population and approximately 2 times that of the general population for females. The mortality among male morons, of all ages, is slightly under that of males in the general population. Among females it is slightly over, the ratio being 1:1. In contrast with the idiot and imbecile groups, morons do not show high ratios in the younger ages.

Important sex differences are noted. Male idiots show extremely high ratios up to the age of 30. Female idiots show still higher ratios than the males, but these decline perceptibly after the age of 20. In imbeciles the sex differences are not marked, both groups presenting ratios which are high for the first two decades, reaching stability at the age of 20. Among the morons, the females present a higher total ratio, and this is observed particularly in the first two decades. Male morons present a lower total ratio. Very few differences are noted between the various age groups.

The mortality in all mental groups considered together, compared with that of the general population gives a ratio of 2:3 for males in all age groups (from 2 to 59 years). For females the ratio is 2:1.

The tendency is for female mental defectives to die under the age of 20, but those who survive have a fairly good chance of living to older ages. Male mental defectives do not die as rapidly under the age of 10, but have a higher death rate than the females throughout the remaining years of the life span.

In a comparison made between the United States census study of 1,347 deaths in institutions for mental defectives throughout the United States during the year 1922 and the present Massachusetts study of 878 deaths over a fourteen year period, in all groups combined the United States census study recorded a death rate per thousand persons under treatment of 32.2 for males and 24.8 for females. The rate in Massachusetts was 20.5 for males and 16.2 for females.

Starting with 1,000 live births it was estimated that in Massachusetts 803 males survive in the general population at 10 years, 705 morons, 314 imbeciles and 276 idiots; for females the number surviving in each group would be 831 of the general population, 722 morons, 387 imbeciles and 268 idiots, or, by combination of the total number of cases in the three groups, the average survivorship of all mental defectives at 10 years would be 325 males and 341 females.

The most important causes of death among mental defectives are: influenza, 16 per cent; pulmonary tuberculosis, 14 per cent; other forms of tuberculosis, 4 per cent; bronchopneumonia, 8 per cent; lobar pneumonia, 7 per cent; diseases of the heart, 6 per cent; epilepsy, 4 per cent; diarrhea, 4 per cent, and measles, 3.9 per cent.

In an analysis of 1,000 consecutive deaths at the Earlswood Asylum, England, Tredgold found that tuberculosis (all forms) was the cause in 39.6 per cent of the total deaths. Next in order came epileptic convulsions and pneumonia.

Diseases present different ratios for the various age groups. For instance, in diarrhea and diseases of the heart the ratios are comparable for all of the age groups. In epilepsy, bronchopneumonia, lobar pneumonia and tuberculosis of the lungs the ratios are very high in the first decade, lower in the second decade and still lower but comparable for the remaining age groups. The same tendency to high ratios in the younger ages with smaller differences between the remaining age groups is seen in influenza and nephritis. The highest ratio is found in epilepsy which presents the following ratios for the different age groups: from 2 to 9 years, a ratio of 140; from 10 to 19 years, 13; from 20 to 29 years, 8; from 30 to 39 years, 20 and from 40 to 49 years, 30.

The average expectation of life for a boy of 2 years in the general population in Massachusetts is 56.8 years. For idiots this figure is reduced to an average expectation of 20.1 years; for imbeciles, 29.6 years; for morons, 52.2 years, and for mentally defective males as a whole, 30.1 years. For a girl infant of 2 years the average expectation of life is 59.3 years; for idiots, 21.3 years; for imbeciles, 38.4 years; for morons 46.8 years, and for all mentally defective females, 32.9 years. (Patients under 2 years of age are not admitted to the Massachusetts institutions used in this study.)

GENGENBACH, Denver.

TANTRUM SPASMS. R. DEBRÉ and F. LÉVY, Nourrisson **20**:73 (March) 1932.

Tantrum spasms always follow a fit of crying, and unless one is familiar with them they may be confused with convulsions from other causes, e. g., epilepsy,

hyperpyrexia and especially spasmophilia. Babies who have these spasms show evidence of nervous instability from early infancy; many are breath holders.

The first attack usually occurs between the ages of 6 months and 1 year. Fourteen cases are reported. The treatment is unsatisfactory, but the ultimate prognosis is excellent. The differential diagnosis is the most important feature in this disease.

McCLELLAND, Cleveland.

CHOREA AS DIAGNOSED BY HANDWRITING. PAUL KARHER, Monatschr. f. Kinderh. **53**:197, 1932.

This article affords an interesting study of different specimens of handwriting in cases of chorea. The involuntary, spontaneous movements in the smaller muscles are shown by lines on the paper perfectly independent of the word the child is writing. The writer believes that chorea can often be diagnosed more readily by these findings than by physical examination.

GERSTLEY, Chicago.

PURULENT MENINGITIS IN EARLY INFANCY. EUGEN STRANSKY, Monatschr. f. Kinderh. **53**:235, 1932.

The writer reviews the literature, reminding us that the younger the nursling, the less evident are the symptoms of purulent meningitis. Frequently the disease causes no manifestations and is suspected only after the development of a resulting hydrocephalus.

Stransky then quotes the case of a 5 weeks old baby who had already shown symptoms of rapidly developing hydrocephalus. Punctures of the fontanel showed purulent fluid. He believes that this was a case of prenatal meningitis.

GERSTLEY, Chicago.

CURING INJURIES OF THE SPINAL CORD IN EXPERIMENTAL RACHIOTOMY OF THE FETUS. ANGELO MIGLIAVACCA, Ztschr. f. Geburtsh. u. Gynäk. **101**:184, 1931.

The author made experiments proving that regeneration of the nerve fibers of the spinal cord is possible after complete division. Good results were obtained during the last years in low vertebrates. However, no investigator as yet has accomplished a regeneration and return of the function in mammals. The author made his experiments on mice and rats at a very early stage of pregnancy. He describes the operation of rachiotomy on the fetus *in utero*, a rather difficult operation. He could observe a real and complete regeneration of the nerve fibers in several cases. The recently published experiments of Hooker and Nicholas from the University of Pittsburgh are thought to be valueless as far as the microscopic observations are concerned, due to wrong technic.

ADAIR and SIEDENTOPF, Chicago.

THE SUCKING REFLEX. N. J. BALIASSNIKOWA and M. M. MODEL, Ztschr. f. Kinderforsch. **39**:1 (Oct. 19) 1931.

The sucking reflex is a complicated, unconditional chain reflex. It begins to function immediately after birth not only in full-term but also in premature children. The authors discuss different stages of the mechanism. It is probably under the control of the midbrain and in particular of the corpus striatum. During the period of sucking the vegetative nervous system is stimulated.

REICHLE, Cleveland.

PSYCHASTHENIA. THEODOR HELLER, Ztschr. f. Kinderforsch. **39**:17 (Oct. 19) 1931.

Heller describes in detail a form of psychopathy in which he has been interested for many years. Persons suffering from psychasthenia do not possess the normal

ability to conquer the inhibitions produced by disagreeable sensations. This leads to a fear of everything disagreeable and influences the will and actions of the patient. This temperament shows its first signs in early childhood. The children do not develop the normal love of play; their facial expression betrays their disagreeable sensations. The frequent shrieking and crying, which is not activated by any reasonable external cause, is quite characteristic of them. These children have no affection for any one. They are notoriously poor eaters. Their anorexia, however, leads to no great loss of weight. Suddenly they begin to eat again; no permanent damage is done by their period of semistarvation. Heller, however, points out that these periods of voluntary deprivation from food have a great influence on the character of the child in that the child learns that it can control its surroundings by such conduct. The attitude of defiance characteristic of children from 2 to 4 years (Benjamin) is strikingly emphasized in the psychasthenic child; he is asocial and isolates himself from any larger group.

Often the psychasthenic child is unusually intelligent. The innate intelligence, however, is inhibited so strongly by the feelings of disgust and dislike, and the energy which the individual must develop to overcome these abnormal inhibitions is so great that the actual results of his work do not correspond with his capacity. In school these children often test the patience of the teacher. They demand a great deal of personal attention. Heller points out that many of the cases of suicide in children and young adults are drawn from this group; instead of commiting suicide, these children may pass into a psychasthenic crisis. These are periods of extreme irritability and paroxysms of almost maniacal activity, when the psychasthenic child submits entirely to his character defect and attempts to revenge himself on persons whom he believes are disagreeable to him. During these attacks the child may act in such a fashion as to awaken suspicion of serious mental disease.

Despite the fact that this form of psychopathy is undoubtedly due to an endogenous defect, Heller believes that it is possible to restore these patients to normal life by the proper pedagogic training. He has known a number of such persons who have returned to normal existence and have succeeded in conquering their temperamental defects despite disadvantageous external circumstances. The principle of this training is to bring the child into an environment from which all sources of disagreeable stimuli are eliminated and then cautiously to train him to acquire character control and self-discipline.

REICHLE, Cleveland.

THE ACUTE CEREBRAL TREMOR OF ZAPPERT. J. G. SCHEWTSCHENKO, Ztschr. f. Kinderforsch. **39**:40 (Oct. 19) 1931.

This disease, which is characteristic of early childhood, was first described by Henoch in 1881 and studied by Zappert in 1909. It is comparatively rare. Children under 2 years are most often affected. The most important symptom is the tremor that affects the entire body. It may be rhythmic, or it may even approach the type of an intention tremor. The sickness may start with coma; nystagmus, meningitis, general rigidity, discoordination and paralysis of the facial nerves may occur. The prognosis is usually good, and restoration of function may be complete.

The author saw three cases, in a mother and two children. One of the children died; the results of the autopsy are published. The important features of this examination are as follows: hemorrhagic meningitis; a diffuse, toxic change in the nerves and glia of the brain and a periadventitial infiltration of the gray matter of the ventricles. The condition is probably one of the forms of encephalitis.

REICHLE, Cleveland.

EPIDEMIC CEREBROSPINAL MENINGITIS IN CHILDREN AND ITS CLINICAL THERAPY. N. M. FRISHMAN, Oxmat. i Ozdp. **2**:24, 1931.

Among the diseases of children cerebrospinal meningitis occupies a very important place, if not in frequency, in severity. Of all the cases of cerebrospinal

meningitis, from 80 to 85 per cent occur in children. The main cause is the meningococcus. Any chronic or subacute infection around the ear, nose or throat may predispose to this disease.

The most prominent symptoms in children are a rash, polyarthritis, vomiting, weakness, diarrhea and rigidity of the neck. In infants the diagnosis is difficult. The early symptoms are tension in the fontanels, restlessness, photophobia, a desire not to be touched, semiconsciousness and the presence of Babinski's, Brudzinski's and Kernig's sign.

The author uses the following treatment in these cases with good results: serotherapy, methenamine administered intravenously, hot baths, lumbar puncture, vaccine therapy and autotherapy.

KRUPINSKI, Chicago.

NERVOUS CHILDREN AND THE ONLY CHILD. P. P. PHRANTZOV, Pediatriya **14**:381, 1930.

Nervous children are not a rare phenomenon. It is Dr. Diakov's estimate that 75 per cent of the children in the schools of Russia are nervous. This article sums up the results of a study conducted on two hundred and twenty-nine children of preschool and school age in children's homes and schools.

The nervous child possesses certain definite characteristics, which are distinguished in the early days immediately after birth. The symptoms are as follows: There is constant movement of the body; during the feeding there are restlessness and interruptions, frequently accompanied by vomiting; the elimination is changeable, in most cases liquid, and at times both solid and liquid on the same day. In the first instance the quantity is small; in the latter, large.

The condition of the child between 5 and 14 months of age is as follows: There are again useless muscular movements of the body and strong reactions to outside stimuli, and the child begins to walk at an early age (from 6 to 8 months). Nourishment is far below normal, due to peevishness and lack of appetite, and is subject to the influence of atmospheric conditions, which are reflected in the temperature of the nervous child's body. A high temperature is also caused by slight provocations and emotional excitement, such as anger and fear, and results in convulsions. The child's resistance to infection is lowered.

At the age of from 2 to 3 years the child speaks well and clearly. Sleep is restless and marked by grinding the teeth and crying. The awakening of the sexual instinct, curiosity, a desire to touch the sexual organs and finally masturbation are detected at this early age. At the age of from 4 to 5 years the symptoms are more pronounced and varied. The child's mental development is striking, its thirst for new experiences causes its state of mind to change quickly from that of depression to enthusiasm. Speech is rapid and stuttering. With the approach of school age the habitus of the child is especially characteristic. The contours of the body are described by Dr. Cameron. The condition of the nervous child's body is the direct antithesis of the body well developed by military exercise. These exercises are conducive to development of the so-called "military" virtues, such as resistance to weariness and accuracy of movements. The weakness of the nervous child is the result of the absence of these valuable qualities. Its body is held up not so much by muscular tension as by the balance of the body striving to retain its position. As a result, the curves of the spinal column are exaggerated. The exceedingly pronounced lordosis throws the shoulders back and brings out the abdomen. A compensating curve of the spinal column in the region of the neck is necessary to bring the sight in line with the rest of the body. The chest is flat, soft and easily indented. A paleness of the skin and acrocyanosis of the extremities simulate anemia. Although the heart, lungs and other internal organs show no pathologic indication, the dry cough frightens the parent, and young doctors are inclined to make a diagnosis of tuberculosis. Owing to subnormal digestion, the appetite is impaired; this impairment ordinarily lasts to sexual maturity. Psychically the nervous child is one-sided, lacks ability to concentrate,

wearies, fears animals and darkness, thirsts for change of impressions and pleasures and shows a marked tendency toward egocentricity.

The cause of nervous children has not been clearly established. It has been observed, though, that an only child in a family as a rule has the pathologic symptoms enumerated in the foregoing paragraphs. One theory contends that these neuropathologic symptoms of children clearly manifest the disturbance of the vagotonic nervous system. Hypertonia among children of early age, stomach aches and restlessness are typical indications of vagotonia. Dr. Littman, in *The Journal of the American Medical Association,* related his experiences in treating nervous children with atropine. At first the patients were subjected to a treatment that does not act on the vagotonic nervous system. Then small doses of atropine were administered to the children. Of the fifty-nine children, forty-four gave satisfactory results, and in twenty-four the results were effected so swiftly as to indicate a specific action.

Another theory seeks to explain neuropathologic conditions in children by the order of birth. Dr. Steel observes that the greatest percentage of sick children and children born dead is among the first-born. He explains this by stating that the mother's system is not so favorably fitted for the healthy development of the child when the first child is born as when the second or third child is born. In these days when mothers pride themselves on the "first and last child," it is easy to account for the large percentage of nervous children. Parents, unduly careful of the welfare of the only child, refuse it the normal associations with other children that are so necessary for the development of a healthy, normal, social personality. The whole atmosphere of modern life is one of congestion; its fast tempo and unnaturalness are fertile ground for the growth of the neuropathic child.

The problem of the nervous child is not only medical; it is also all-important sociologically. The method of combating the problem is twofold — prophylactic on the one hand and therapeutic and pedagogic on the other.

Parents must be given to understand that a normal family, brothers and sisters with whom the child can associate normally, are important in the development of a socially valuable individuality.

Among therapeutic treatments of nervous children the physiodietetic is most important. The child must be exposed to sunlight and fresh air; he must take exercises. Nourishment should be administered to him without force. The diet should be based on carbohydrates and albumins. In case the appetite shows improvement, fats may be added in small amounts.

In school all effort should be directed toward the elimination of the negative characteristics of the nervous child; this has to do with the problem of instilling responsibilities and developing qualities of social value — character, will, self-confidence, ability to cooperate with others and similar traits that go to make up a socially valuable personality.

YAMPLOSKY, Atlanta, Ga.

Diseases of the Ear, Nose and Throat

ABSORPTION OF FOREIGN MATTER IN TONSILS: I. EXPERIMENTS WITH ARSPHENAMINE ON HUMAN TONSILS. G. KELEMEN and A. HASSKÓ, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **130**:318 (Feb. 25) 1932.

Kelemen and Hasskó report the first of two series of experiments investigating the absorption of foreign matter in the tonsils. The tonsils of young persons, which had been painted with solutions of arsphenamine a short time before their surgical removal, were examined, after excision, by Jancsó's reduction test. Arsphenamine is conducted toward the lymphoid ground tissue only if the epithelium is intact. In the epithelium there were granular deposits in the protoplasm, especially the nucleus, which has an elective receptivity for arsphenamine preparations. In the lymphoid ground tissue, storage of arsphenamine took place in the framework of the reticulum, the elements of which here appeared as tubular structures with stained walls, or fibrils with incrustations. It is the cells which

ensheath these fibrils or tubular fibers and which the authors call wall cells that constitute the actual storage elements of the reticulum. Blood and lymph vessels, especially the lymph spaces beneath the epithelium, take up the precipitate in the form of thrombi and also in their walls, but rapidly transport it to the underlying tissue. With the intravenous injection of massive doses of arsphenamine (which, however, can be made only in animals), the coarser elastic fibers of the parenchyma showed the strongest imbibition, thereby concealing the finer meshes of the reticular network. The region of the secondary nodules remains free from arsphenamine after painting of the tonsils as well as after intravenous injection, with the exception of occasional small thrombi in the vessels.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OTITIS IN NURSLINGS AND ITS COMPLICATIONS. M. KRASSNIG, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **130**:335 (Feb. 25) 1932.

Krassnig discusses otitis in nurslings and its complications on the basis of otologic examination of 920 nurslings, on 52 of whom autopsies were performed. The author recognizes the frequent existence of a latent otitis, by which he means a condition in which otologic examination shows a diseased tympanum but there are no subjective symptoms, such as fever or pain. Otitis of this latent type, or with slight clinical symptoms, when associated with dyspepsia in nurslings, is usually due to a decreased general resistance resulting from the intestinal disturbance. This view is supported by the fact that the dyspeptic symptoms usually precede the otitic symptoms by weeks or months, and that an improvement in the general condition never results from treatment of the ear, whereas the otitic symptoms usually disappear when the intestinal function returns to normal. A decline in general health cannot be attributed to latent mastoiditis, as a suppuration of the mastoid antrum in a nursling would rapidly become noticeable at the surface or spread inwardly and give rise to endocranial complications. In the 4 cases of endocranial complications in which the possibility of otogenous origin was admitted, clinical findings and sometimes autopsy observations proved this supposition wrong. The author thinks that the otitis of nurslings is not as dangerous as some otologists think or as insignificant as some pediatricians believe. Usually it is only one manifestation of a general disturbance of the organism. Diagnostic paracentesis often helps to determine the clinical importance of the otitis. If there is no secretion following paracentesis or if it stops after a short time and all other local symptoms such as inflammation of the lymph nodes, periostitis and changes in the auditory meatus are lacking, the otitis probably does not play an important rôle in the clinical picture.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SYMPTOM OF COMPLICATION FOLLOWING ADENOTOMY. H. SCHAEFER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **131**:231 (May 23) 1932.

Schaefer reports a symptom of complication after adenotomy which he has observed frequently of late but of which he finds no mention in the literature. It consists in severe circumscribed pain at the nape of the neck, setting in soon after the operation and impeding certain movements of the head. The manifestation usually recedes within a week. There is no pressure sensitivity in the affected part, the lymph nodes at the nape of the neck are not palpable, and other cervical lymph nodes are the same size and consistency as before the operation. The possible theories for the development of this symptom (mechanical, inflammatory and infectious) are critically considered. The most probable explanation in the opinion of the author is that the pain is a symptom of a lymphangitis, or lymphadenitis, resulting from surgical opening of lymph channels and consequent spread of infected lymph thrombi.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CAUSES OF FAILURE IN ADENOID OPERATION. K. BERNFELD, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **131**:234 (May 23) 1932.

Bernfeld thinks that one of the chief causes for the frequent failure of adenoid operations is the lack of consideration given to the variable morphologic peculiarities of the epipharynx. He emphasizes the importance of an accurate examination of the nasopharynx prior to possible operation, and discusses the three most important methods of examination: postrhinoscopic mirror examination, palpation and roentgenologic examination. The importance of diagnosing an infantile nasopharynx, which can lead to a number of disturbances in the region of the ear and pharynx, etc., is stressed. He points out the existence of asymmetries of the pharynx and epipharynx hitherto unnoticed. The choice of curet must be exactly suited to the morphologic conditions of the nasopharynx, whether the operation is performed blindly or under direct visual control. The indication and prognosis of nasal disturbances in the presence of adenoids can be estimated correctly only if the relation between the formation of the nasopharynx and other obstructions of the nasopharynx has been ascertained with clarity.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

NORMAL DEVELOPMENT OF THE HUMAN NOSE, IN PARTICULAR OF THE ETHMOID CELLS. H. RICHTER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **131**:265 (June 22) 1932.

Richter traces the development of the human nose and especially of the ethmoid cells in the embryonic period, month by month and through the postnatal period to the tenth year of life. His article is based on the examination of twelve fetuses of varying ages, one new-born infant and seven children between the ages of 1 and 10 years. It is accompanied by numerous plates.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TRANSITORY CROSSED ABSENCE OF ROTATORY AND CALORIC REACTION IN A CHILD. E. VERMES, Monatschr. f. Ohrenh. **66**:689 (June) 1932.

Vermes reports the case of a child, aged 7, who sustained a slight trauma of the skull. Two days later pains in the throat and ears appeared, and two days after that vomiting and vertigo set in, followed by facial paralysis. Examination in the otologic clinic revealed that all three branches of the right seventh cranial nerve were paralyzed, and that the fifth and ninth cranial nerves on the right side were also involved. The eighth cranial nerve was involved on both sides. On the right the rotatory reflex was lacking; there were slight underexcitability for irrigation with cold water, spontaneous nystagmus of the first degree to the left and a slight decrease in the hearing capacity compared to the normal hearing of the other side. On the left side there were vestibular nonexcitability for irrigation with cold water and normal excitability to rotation. Roentgenologically there were signs of great increase of intracranial pressure, but clinically there was no support for this. With the exception of a slight caloric underexcitability on the right side, the patient exhibited complete spontaneous recovery after two and one-half months. The pathogenesis is undetermined. The author considers the trauma too slight to be the etiologic agent; a cerebral polyneuritis of infectious toxic origin would be more probable. Other possible causes of the symptoms are mentioned.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ARE THERE HARMFUL EFFECTS FOLLOWING TONSILLECTOMY? E. WIRTH and O. LACHENIT, München. med. Wchnschr. **78**:1898 (Nov. 6) 1931.

The authors reexamined ninety-two patients who had had their tonsils removed from one to ten years before, and did not find any harmful effects following the operation. Seventy per cent had no complaints. The others had minor complaints

due to conditions, usually in the nasopharynx or sinuses, that were present before the operation. The patients were asked if they would consent to a tonsillectomy, if they had the choice over again. Practically all answered in the affirmative.

BRAHDY, Mount Vernon, N. Y.

Diseases of the Skin

LUPUS ERYTHEMATOSUS IN INFANCY AND IN CHILDHOOD. CLYDE L. CUMMER, Arch. Dermat. & Syph. **24**:999 (Dec.) 1931.

The author has made an excellent and thorough study of the literature dealing with lupus erythematosus. He includes studies of the literature by other authors, general series of cases, single cases and two cases in patients whom he treated himself. The cases studied, whether single or in groups, were found to be inadequate in description of race, age of onset, type of lesion and result of treatment.

The possible connection with exposure to the sun's rays seems to be generally recognized as a causative or at least as a contributory factor. The incidence of tuberculosis was found to be in about the same proportion as would be found in any study of hospitalized patients.

Lupus erythematosus has been generally regarded as rare in childhood. This is shown to be untrue, as the general series of cases of the disease shows that from 2.3 to 11 per cent occur during or before the fifteenth year of life. The incidence is progressively greater in each five-year period of life, there being seven times as many cases in the period from 10 to 15 years, as in the first five-year period of life.

The disease occurs in the colored as well as the white child. The ratio of females to males is approximately 7:3. The disease may begin during the first year of life and may last many years. The course of the disease in childhood, including the appearance of the eruption and its response to therapy with gold compounds, does not show any striking difference from that in adult life.

HENNING, Iowa City.

A NOTE: THE EPIDEMIOLOGY OF TINEA CAPITIS. G. H. PERCIVAL, Brit. M. J. **1**:93 (Jan. 16) 1932.

A report is furnished of the methods used for the prevention and elimination of tinea capitis in the schools of Edinburgh. Isolation in separate schools is practiced, and treatment is carried out by means of roentgen rays and thallium. It is felt that the incidence has been materially reduced since this procedure was instituted.

ROYSTER, UNIVERSITY, VA.

ECZEMA. G. B. DOWLING, Practitioner **128**:299 (March) 1932.

As defined by the author, eczema is not a disease but a reaction of the skin of a special type, brought about by an infinite variety of causes. Dowling presents the subject with four main headings:

(*a*) He stresses the importance of an accurate knowledge of the histologic and clinical picture and quotes Darier's excellent description: "Spongiosis consists of an intercellular infiltration of plasma in the malpighian body as the result of which the malpighian cells are separated one from another and deformed. Although at first preserving their filaments of union, these eventually rupture; spongiosis is dispersed in little foci more or less closely aggregated, in the center or towards the edges of which may be seen little spaces deprived of cells; these are microscopic vesicles. The large vesicles of eczema visible to the naked eye result from the distention of these foci and the inflation of the smaller vesicles and are usually more or less loculated. The fluid is derived by a process known

as exoserosis from the subjacent capillaries, and in the vesicles and among the malpighian cells are found a variable number of migrating lymphocytes; the vesicles may also contain detached epidermal cells. When secondary infection of an eczema takes place, polymorphonuclear leukocytes become added to the migrating lymphocytes.

"To spongiosis and vesiculation is secondarily added acanthosis, or multiplication of the malpighian cells leading to increase in the depth of the epidermis, particularly in the interpapillary portion, and parakeratosis, or failure of the malpighian cells to keratinize in the normal way so that the superficial cells retain their nuclei. The imperfectly keratinized cells lack the resistant quality of the normal horny layer, become desiccated as the result of exposure to air and form the desquamated scale of eczema. To dermal lesions consist of vasodilatation, edema, and infiltration with mononuclear cells disposed around the cutaneous vessels."

The clinical varieties are often named after their configuration and regional distribution, the author points out, as he carefully describes the following: intertriginous, chronic flexural eczema with lichenification, nummular papulovesicular eczema, eczema in infancy and seborrheic eczema.

(*b*) Under etiology, Dowling divides the causes of eczema into: (1) predisposing causes, the most important being heredity; others noted are faulty hygiene, alcoholism, overwork, nervous exhaustion, digestive disturbances, constipation, chronic colitis, pregnancy, the menopause and diabetes; (2) exciting causes, which are divided into internal and external causes. He takes particular pains to explain the difference between the terms eczema and dermatitis as caused by external irritants, the question of marked susceptibility of a given skin to a given irritant being the determining factor.

(*c*) The pathogenesis of eczema, the writer states, is due to the sensitivity that resides in the epidermis. Under this heading, the eczema-asthma complex, the idiosyncratic eczemas, occupational eczemas, eczema due to physical causes, and microbic and mycotic eczemas are discussed.

(*d*) In treating eczema, Dowling states, careful consideration must be given to general conditions such as rest—mental and physical—to avoidance of stimulants and to diet. The local treatment used must be elastic, varying according to the stage of the disease. Several formulas for local treatment in special varieties of eczema are given.

SAPPINGTON, San Francisco.

RINGWORM OF THE SCALP. W. J. O'DONOVAN, Practitioner **128**:315 (March) 1932.

In this interesting paper, O'Donovan reviews the work and records of the skin department of the London Hospital from 1905 to 1931. During this time, 8,335 patients with ringworm of the scalp were treated. The author points out that this is a diminishing disease as evidenced by the records of the last five years; 196 cases were recorded in 1927, and progressively fewer each year, with only 99 cases in 1931.

As to symptoms, O'Donovan states that itching or discomfort is rarely felt. In the earliest stages there are small areas of pseudobaldness, with fairly definite outlines having a white or gray scaly surface from which project a few short hairs broken off near the scalp. Lesions are usually multiple.

The author outlines in detail two methods of treatment by epilation: by roentgen rays and by thallium acetate.

He stresses the point that the early recognition of ringworm is the chief factor in checking the propagation of this unpleasant malady.

SAPPINGTON, San Francisco.

TRIGEMINAL NAEVUS AND HOMO-LATERAL PIAL ANGIOMA. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **25**:954 (May) 1932.

A boy of 9¾ years, an only child, had suffered from recurrent fits during infancy and at the time of this report suffered from them about every three months. The mother complained that he was deficient and silly. On admission to the hospital he was found to drag his left leg and to trip easily; he was mentally active but backward for his age. The Wassermann test was negative. Over the right side of the face an extensive nevus was present, following the cutaneous distribution of the ophthalmic branch of the fifth nerve. Left external strabismus was present. The roentgenogram of the skull showed two areas of calcification on the right side, one just above the level of the tentorium cerebelli and the other lying in the region of the posterior part of the right parietal bone. The case illustrates the clinical syndrome of jacksonian epileptic attacks associated with a trigeminal nevus.

WILLIAMSON, New Orleans.

TREATMENT OF ERYTHRODERMIA OF LEINER-MOUSSOUS TYPE WITH RAPID CURE. RÔLE OF THE ENTEROCOCCUS. G. BLECHMANN and P. POTELUNE, Bull. Soc. de pédiat. de Paris **29**:469 (Oct.) 1931.

Intense erythema of the buttocks developed in a male infant soon after birth. The condition became more and more extensive. The child had considerable vomiting and frequent loose stools, even though he was breast fed. He was first seen at the age of 2 months when he presented the signs characteristic of a desquamating erythrodermia, as described by Leiner-Moussous. He was markedly athreptic. He was taken off the breast, and was given various feedings, including condensed milk and buttermilk, without any improvement in the cutaneous or in the general condition. He was given injections of the mother's serum, injections of insulin (because of hepatopancreatic insufficiency) and daily doses of anti-enterococcic vaccine by mouth. All applications to the skin were stopped. The patient was seen after five weeks; the skin was practically healed except for a moist intertrigo at the various cutaneous folds, and the general condition was much improved. Cultures made from the intertriginous areas as well as from the stools showed abundance of enterococci (Montlaur). The administration of anti-enterococcic stock vaccine was then begun, and the skin cleared entirely soon afterward. This disease has a considerable mortality, according to the authors. In the discussion some of the speakers agree that this type of skin disease has a high mortality, while others think that the infants that die do so from complications and not from the disease. There is also no definite agreement among the discussers as to the relationship of this type of cutaneous condition to seborrheal eczema and ordinary infantile eczema.

BENJAMIN, Montreal, Canada.

INFLUENCE OF POTASSIUM ON PRURITUS. J. SAUER, Deutsches Arch. f. klin. Med. **172**:219 (Dec. 21) 1931.

Following the observation that potassium bicarbonate or potassium acetate relieved the symptoms in a case of "symptomatic pruritus," Sauer tried treatment with potassium compounds in nine persons with chronic lichen urticatus. These patients were given, three times daily, a tablespoonful of a solution composed of liquor potassi aceti, 30 cc. and aqua destillata, sufficient to make 200 cc. In seven of the nine persons, healing progressed satisfactorily. Several cases of chronic eczema of the hands also yielded to this treatment.

DOOLEY, Kent, Conn.

MODE OF ACTION OF POTASSIUM. J. SAUER, Deutsches Arch. f. klin. Med. **172**:223 (Dec. 21) 1931.

Oral administration of large doses of potassium acetate causes an increase in the potassium content of serum and cerebrospinal fluid. The serum calcium soon

increases also, the ratio of calcium to potassium remaining unchanged. Sodium is displaced from the serum. The disappearance of the pruritus is not dependent on an increase in the potassium content of the blood serum.

DOOLEY, Kent, Conn.

FRAMBESIA IN CHILDHOOD. S. TAKASAKI, Jahrb. f. Kinderh. **134**:169 (Jan.) 1932.

This is a well illustrated description of the disease, based on the author's experiences of ten years in the islands of the South Seas.

CLAUSEN, Rochester, N. Y.

ERYTHEMA NODOSUM IN SCHOOL CHILDREN. A. WALLGREN, Kinderärztl. Praxis **2**:485 (Nov.) 1931.

When a child becomes infected with tuberculosis, it is from three to seven weeks before sensitivity to tuberculin develops; fever ensues, and roentgen examination of the chest shows greater or less thickening near the hilus. At this stage of primary tuberculosis, erythema nodosum develops in a certain percentage of infected children. By carefully examining the contents of the stomach in twenty-seven school children with erythema nodosum, Wallgren found tubercle bacilli in 44 per cent. According to whether the roentgen findings in the lungs were mild, medium or extensive, the positive results of gastric lavage were respectively 10, 50 and 85 per cent; that is, the greater the involvement of the lungs, the greater were the chances of finding tubercle bacilli. Children with erythema nodosum, if the roentgenogram shows slight involvement of the lungs, should be kept from school for approximately one month. Children with more extensive involvement should be isolated for six months, in order to prevent infection of their schoolmates.

HUENEKENS, Minneapolis.

ERYTHEMA NODOSUM. H. ERNBERG, Finska läk.-sällsk.handl. **74**:164 (Feb.) 1932.

The author studied the relation of tuberculosis to erythema nodosum in more than 200 cases. In one series of 39 consecutive cases all of the patients were found to have tuberculous foci, particularly in the pulmonary area. He regards the erythema nodosum as an autogenous allergic manifestation of tuberculosis elsewhere in the body. All patients with erythema nodosum should receive roentgen examination, in order to detect any foci of tuberculosis. Erythema nodosum points to tuberculous infection among immediate contacts and in this respect may be regarded as a warning signal. The prognosis of tuberculosis associated with erythema nodosum is usually good.

ELGHAMMER, Chicago.

Surgery and Orthopedics

SUBPHRENIC ABSCESS. E. P. MCNAMEE, Am. J. Roentgenol. **24**:125 (Aug.) 1930.

The author presents a series of subphrenic abscesses, several of which are in children. He discusses the etiology, anatomy, pathology, histology, physical signs, roentgen observations, course and treatment. He advises against the use of the exploratory needle, as a dangerous practice. Subphrenic abscess is not an uncommon complication following surgical procedures or acute inflammatory conditions of the abdomen. Proper roentgen examination with accurate interpretation is the most important single factor in the diagnosis. Correlation of the roentgen findings with the clinical evidence is important and necessary in the diagnosis of most of the cases. A high fixed diaphragm is present in most cases, but slight excursion does not rule out an abscess. Early diagnosis and proper surgical

treatment will reduce the mortality rate at least 50 per cent. In general, in the stage of diffuse inflammation, drainage through the abdomen gives the best results. After the abscess has become localized (usually from the eighth to the fourteenth day), the transpleural method is advisable.

STULIK, Chicago.

SARCOMA OF THE PROSTATIC AREA IN AN INFANT AGED FOUR MONTHS. GERARD RAAP, Am. J. Roentgenol. **24**:185 (Aug.) 1930.

Of 252 primary tumors reported in the bladder in all ages by Albarran only 6 were in children under 10 years of age, the majority of these occurring in children from 4 to 5 years old. Concetti reported a sarcoma of the bladder in a girl of 11 months. Sarcoma of the bladder was first reported by Stafford in 1839, and about 100 cases are estimated as the total number reported. In an infant with an unimportant family history, except that a brother died at 6 weeks of age with uremic fever (general edema and anuria), strangury developed at the age of 3 months. An abdominal tumor was found by the mother on massage for colic after the physician diagnosed "teething" as the cause of the condition. Catheterization with a filiform and examination revealed an enormously dilated bladder and a prostatic tumor with lateral lobes. At operation a mass, 20 by 15 by 30 mm., was diagnosed myxosarcoma of the prostate. Postoperative recovery was progressive, but after several weeks uremic convulsions appeared, with death taking place in four days. The author feels that irradiation may be the procedure of choice in tumors of this type, even though recurrence within six weeks is reported by others. Cystographic methods are invaluable in making the diagnosis.

STULIK, Chicago.

INTRAVENOUS UROGRAPHY. WILLIAM F. BRAASCH, Am. J. Roentgenol. **25**:196 (Feb.) 1931.

The author reviews the history of intravenous urography and discusses its uses and limitations. His conclusions are: Intravenous urography offers a valuable addition to means of diagnosis of diseases of the urinary tract; it may lead to diagnosis without necessity of cystoscopic data; the greatest value will be in cases in which cystoscopy and ureteral catheterization are contraindicated or impossible; urography will be valuable in children; it will be of great value in the presence of urinary stasis; a weakness lies in that it gives a poor outline of minor deformities; failure of renal visualization does not necessarily indicate that renal function has been destroyed; urography is of value as a visual functional test and often will suffice to determine the presence of a good kidney on the opposite side from that to which symptoms are referred; and organically combined solutions of iodine offer the best results in retrograde pyelography.

STULIK, Chicago.

PARTIAL GASTRECTOMY FOR LYMPHO-SARCOMA IN CHILDHOOD. V. C. HUNT, Ann. Surg. **96**:210 (Aug.) 1932.

The author reports in detail the case of a boy, 3 years and 8 months of age, on whom a partial gastrectomy was performed for lymphosarcoma. The boy had been perfectly well until three weeks before admission to the hospital. The first symptom noted was vomiting. About nine days later, a mass became palpable in the upper part of the abdomen. When admitted to the hospital, he had lost 4 pounds (1,800 Gm.) and was somewhat emaciated and dehydrated. A large, dilated stomach could be outlined, and a mass was palpable at the pylorus; otherwise the physical examination gave negative results. A portion of the stomach was resected, and the child was dismissed from the hospital on the fifteenth day. Subsequent roentgen therapy was carried out.

A review of the literature shows that less than 400 cases of sarcoma have been reported, and the author believes that his patient is the youngest in whom successful gastrectomy has been performed.

BANTIN, Omaha.

ACUTE PERFORATIVE APPENDICITIS IN AN INFANT. D. SWARTZ, Canad. M. A. J. **27**:58 (July) 1932.

The patient, a girl, aged 23 months, had a history of three definite attacks of pain and vomiting, previous to the present attack. The first attack occurred at the age of 11 months. At the time of examination the patient showed signs of acute perforative appendicitis. Operation was performed at once, and an appendix with a large perforation at the base was found. There was free pus in the abdominal cavity. An uneventful recovery ensued.

MOORE, Omaha.

SURGICAL CONDITIONS IN CHILDHOOD. HERBERT E. COE, J. Pediat. **1**:245 (Aug.) 1932.

The author discusses briefly the most recent contributions to the surgical treatment of the following conditions in children: pyloric stenosis, congenital duodenal obstruction, congenital epulis, undescended testis, skull fracture, spina bifida, osteomyelitis of the jaws, empyema, intussusception, pyelitis, enlarged thymus, umbilical hernia, hemangioma, burns and Hirschsprung's disease.

This is a review of recent literature and does not lend itself well to abstracting.

LEMASTER, Evanston, Ill.

PRIMARY OSTEOMYELITIS (CHRONIC FIBROUS) OF THE ANTERIOR SUPERIOR SPINE OF THE ILIUM. R. C. ROBERTSON, South. M. J. **25**:825 (Aug.) 1932.

The case reported occurred in a white boy, 13 years of age. Roentgenograms revealed a small area of destruction which involved the lateral aspect of the left anterior iliac spine. The density of the adjoining bone was moderately increased. Malignant involvement was at first suspected, but as there was no response to deep roentgen therapy, an exploratory operation was performed.

The periosteum overlying the tumor was about twice the ordinary thickness and adherent to the underlying bone. The anterior bone of the crest extending backward from the spine was markedly thickened. The entire area of involvement was sclerotic. From the cultures made at the time of operation, a pure strain of Staphylococcus aureus was recovered.

Complete recovery of the patient followed.

SCHLUTZ, Chicago.

DIAPHRAGMATIC HERNIA. J. BASIL HUME, Brit. J. Surg. **19**:527 (April) 1932.

Diaphragmatic hernia may be simply classified into: (1) the congenital form and (2) the acquired form (nontraumatic and traumatic). Congenital diaphragmatic hernia is defined as a protrusion of some of the abdominal contents through a congenital defect in the diaphragm. There are three types described.

1. Hernia through the pleuroperitoneal membrane, which is due to failure of the closure of the median and dorsal portions of the pleuroperitoneal membrane. In the majority of cases, when a hiatal defect is present, the greater part of the intestine lies in the pleural cavity. The large intestine lies to the left of the small intestine in the position occupied before rotation of the intestine took place. The stomach is sharply bent over to the left and drawn up into the thorax, and there is no hernial sac. This herniation takes place about the end of the second intra-uterine month.

2. Hernia through the dome. This is probably due to rupture or destruction of a portion of the membranous diaphragm. It is placed between the left trefoil of the central tendon anteriorly and the muscular portion posteriorly and laterally. The aperture is rounded or oval with its long axis placed transversely, and there is usually no hernial sac. The stomach and portion of the colon are invariably

herniated, but the spleen, a small portion of the intestine and a greater part of the large intestine may be intrathoracic. The position of the defect corresponds with the level of the entrance of the phrenic nerves into the diaphragm.

3. Hernia through the esophageal orifice: (*a*) Thoracic stomach is due to failure of the caudal migrations of the stomach to keep pace with the descent of the other organs and results in varying portions of the fundus and body of the stomach lying in a peritoneal sac in the posterior mediastinum. The esophageal orifice is consequently enlarged to accommodate the stomach which passes through it. (*b*) In para-esophageal hernia there is a protrusion of the lesser sac of the peritoneum passing through the orifice to the right of the esophagus, and it extends upward into the posterior mediastinum. The sac varies in size from a small finger-like process to a dilated sac of considerable dimensions.

Acquired diaphragmatic hernia is described as follows: 1. Nontraumatic cases are due to two causes, either the gradual protrusion of a hernial sac through a relatively weak spot in the normally developed diaphragm, or the production of an acquired defect, owing to the rupture of some of the muscle fibers at their point of insertion in the central tendon.

2. Any tearing of the muscle fibers by the penetration of a fractured rib, a muscle or a weapon is liable to produce either immediately or later a traumatic diaphragmatic hernia, which in the great majority of cases will be devoid of a hernial sac.

SUMMERFELDT, Toronto, Canada.

FURTHER STUDIES IN INTRAVENOUS PYELOGRAPHY. R. J. WILLAN and JAMES H. SAINT, Brit. J. Surg. **19**:622 (April) 1932.

This article consists of the history of development of methods to outline the interior of the urinary tract and some interesting case reports. In the conclusion, the authors state that they believe that the future of intravenous pyelography is one of distinct promise, though at the present time intravenous pyelography is often disappointing, owing largely to its uncertain results. In some cases, particularly when there is obstruction to the outflow of urine down the ureter, it is likely that intravenous pyelography will often give more information then ureterocatheter pyelography.

SUMMERFELDT, Toronto, Canada.

UNUSUAL INJURY OF THE BONE IN A CHILD. W. HUNTER, Brit. M. J. **1**:658 (April 9) 1932.

This is a report of an unusual injury of the bone as a result of the child's swinging his arm with a spade in his hand.

ROYSTER, University, Va.

SPINAL ANESTHESIA IN CHILDREN. J. SALAZAR DE SOUZA, Arch. de méd. d. enf. **35**:441 (Aug.) 1932.

In a series numbering 540 cases, of which 62 were in children under 2 years of age, the author used spinal anesthesia for various surgical conditions. Contrary to his experience among adults, Souza found that cephalalgia, vomiting, painful stiffness of the spinal musculature and paresis of the bladder were extremely uncommon. The youngest patient was a baby, 1 month of age. Meningitic reactions following the use of 5 per cent procaine hydrochloride-epinephrine are aseptic and transitory. Further conclusions from this study show that the benign character of the anesthesia bears an inverse ratio to the age of the patient and that the smallest quantity employed facilitates more rapid elimination. This fact and the greater tolerance in infancy constitute the agencies that make even the youngest patients ideal subjects for spinal anesthesia.

AMESSE, Denver.

CONSERVATIVE TREATMENT OF MUSCULAR TORTICOLLIS. M. KOLLMANN, Med. Klin. **28**:296 (Feb. 26) 1932.

Congenital forms of torticollis with or without asymmetry of the face and skull are treated by the author with conservative methods. Starting in the fourth week of life the infants are trained to lie on a hard mattress, face down. Gradually passive turning of the head and stretching of the neck is carried out in this position. With these simple methods the author has seen very satisfactory results in eighteen cases during the past three years. ZENTAY, St. Louis.

SEVERE BURNS IN CHILDHOOD. B. OSTROWSKY, Monatschr. f. Kinderh. **54**:73, 1932.

In the treatment of eleven cases of severe burn, the author obtained favorable results by using treatments which completely coated the surface and kept the parts sterile. For this he used combinations of picric acid in alcohol, 5 per cent tannic acid ointment and a paste of bismuth subgallate, U. S. P. These dressings protect the injured parts from pain and should be left in place for about three weeks.

In severe burns of the third degree in which there is necrosis in the deeper tissues that cannot be prevented by the superficial dressing and in which histamine is probably being formed, he recommends the permanent bath.

GERSTLEY, Chicago.

Miscellaneous

THE USE OF THYROID AND SUPRARENAL IN THE DIATHESES OF INFANCY. ORVILLE BARBOUR, Illinois M. J. **61**:345 (April) 1932.

There is much clinical and laboratory evidence that the constitutional diatheses of infancy are manifestations of a neurochemical imbalance of the congenitally unstable physiologic activities of the infant. There is some pathologic and clinical evidence that this neurochemical imbalance is the result of a disturbed equilibrium between the secretions of the endocrine glands. Therapeutic results, which are presented for confirmation, infer that the endocrine dysfunction lies primarily in the thyroid and suprarenal glands. During the past two years the author has found that the gastro-intestinal symptoms (vomiting, intestinal colic, flatus and constipation) of diathetic infants are usually promptly relieved following administration of thyroid. In each case with respiratory and circulatory symptoms (laryngeal stridor, dyspnea, coughing, breath-holding and cyanosis), almost immediate benefit follows the administration of suprarenal gland extract, and subsequent permanent relief occurs with its continuance. Those cases showing both respiratory and digestive symptoms respond favorably to combined thyroid and suprarenal therapy. The nervous irritability which is frequently seen in these infants is allayed following thyroid treatment. The suprarenal therapy seems effective for the eczematous cutaneous lesions that are present in a certain number of these babies. Each of these glandular substances appears to have some synergistic effect on the other.

AUTHOR'S SUMMARY.

CHILD STUDY AND THE PEDIATRICIAN. JESSE R. GERSTLEY, Illinois M. J. **62**:27 (July) 1932.

Gerstley reminds the pediatrician that the child study movement is new and that it, like infant nutrition, may undergo a decided evolution. He urges pediatricians to take cognizance of this new movement and to assimilate what is good and essential, so that they may be equipped to answer intelligently questions that are asked them and to refute much of the nonsense that is being promulgated.

BARBOUR, Peoria, Ill.

THE AMERICAN ACADEMY OF PEDIATRICS: WHY AND WHAT FOR? JOHN LOVETT MORSE, J. Pediat. **1**:1 (July) 1932.

Pediatricians are urged to cooperate with professional and lay organizations interested in children's welfare and to assist in the follow-up work of the White House Conference on Child Health and Protection. The author emphasizes the need of teaching the human side of pediatrics and suggests more beside pediatrics rather than too much laboratory instruction. He recommends short courses for graduates and extension courses to inform physicians now in practice of the progress being made in pediatrics. The members of the Academy are urged to be leaders, to teach by the good example they set and not to be misled by fads and new methods proposed by commercially-minded manufacturers. A plea is made to discourage the useless and unproductive research done by those unsuited, but for men genuinely of the scientific and investigative mind to furnish "puddles, ponds and lakes" according to their size and ability. The objects of the American Academy of Pediatrics are primarily altruistic and are, in brief, to improve the health and welfare of children, to raise the standards of pediatric education and practice and to encourage research in pediatrics.

LEMASTER, Evanston, Ill.

ACCOMPLISHMENTS OF PREVENTIVE MEDICINE. E. STARR JUDD, J. South Carolina M. A. **28**:157 (June) 1932.

Some have called this the biologic age, and emphasis is being placed on genetic knowledge and on eugenics in the field of preventive medicine. The average age of death in the year 1800 was 33 years; in 1901, it was 49.2 years, while in 1924 it was 58.1 years. The death rate from all causes in the first year of life has decreased from 17.5 per thousand in 1900 to 12 per thousand.

Judd reviews the infectious diseases, stating how tuberculosis has fallen from first to fifth place among the causes of death. The incidence of typhoid has been lowered by the use of typhoid vaccine. Diphtheria is well controlled by antitoxin and is being eradicated by the employment of toxin-antitoxin or toxoid. Scarlet fever and measles take their toll to a much less extent than formerly, and he predicts that in a comparatively short time the epidemics will disappear. Syphilis will be eradicated in time in civilized countries.

The outstanding problems of health of the present day are four: (1) heart disease, with its associated conditions or apoplexy, cerebral hemorrhage and nephritis; (2) cancer; (3) pneumonia, and (4) mental illness.

Judd lays stress on periodic examinations, particularly for cancer and circulatory disturbances, but these are not of great importance to the pediatrician; however, pneumonia and mental illness play important rôles. Six per cent of those who are mentally deficient have had an accident or injury at birth. Twenty-eight per cent have had acute illness or severe injuries in early infancy or childhood. Probably the mental deficiency of 25 per cent is the result of heredity, and in probably 10 per cent, mentally deficient mothers account for the condition of their children. From this report it is evident that if we can reduce the number of accidents and injuries at birth, we can prevent a certain amount of mental illness.

More has been done in preventive medicine in the past twenty-four years than in the previous twenty-four centuries.

WESTON, Columbia, S. C.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Regular Meeting, Dec. 8, 1932

JOHN CAFFEY, M.D., *Presiding*

VALUE OF LARGE SECTIONS OF THE LUNG IN PATHOLOGIC STUDY OF PNEUMONIA. DR. CHARLES HENDEE SMITH, DR. IRVING GRAEF and DR. ELIZABETH TORREY ANDREWS.

In the study of pneumonia which has been under way for the last seven years in the Children's Medical Service of Bellevue Hospital, it early became evident that the small section of the lung taken in the usual routine gave no adequate information about the lesions. Under the older methods it was necessary to take several blocks from different parts of the lungs, selecting these by the gross appearances or by density on palpation. But this gave one only a fragmentary conception of the relation of the various lesions found in the different sections. Our later experience has proved that it is difficult to ascertain the presence of bronchopneumonia by gross examination, and therefore that it is possible, if blocks are taken only from areas that seem abnormal to sight or touch, to miss entirely an extensive early lesion.

In the past three years a technic has been devised by which, in the case of a young infant, sections can be made large enough to include a whole lobe or even a whole lung. Large thin blocks are taken, embedded in paraffin and cut on a pyroxylin microtome. After much experimentation, Mr. Edgar Nebel, the technician, has worked out a method by which sections from 8 to 12 microns thick can be cut.

The plane of the sections is important. Because of the desirability of comparing the section with a roentgenogram, the first section is taken in a frontal plane running directly outward from the hilus. Thus the main bronchi and the bronchopulmonary nodes are included, as well as the parenchyma of the lung. But since many lesions of the lung are confined to the posterior portions, it is desirable to take a second section parallel to the first but nearer the posterior surface of the lung. In some cases it is well to take anteroposterior sections in addition, but these are less often useful than the first two.

These large sections show the distribution of the lesions through the lung. The lesions often vary greatly in character in various parts of the lung or even of the same lobe. Lesions unsuspected in the gross examination are frequently found in a study of the whole lung under the microscope. These thin sections are much better than thick slabs, since they may be studied under high power magnification at any time. When mounted directly on lantern slides, they may be shown in the ordinary projector. Even though the magnification may not be high, much of the pathologic process may be demonstrated in this way.

More then ninety cases have been studied by means of the large sections. The clinical course and the roentgen findings have been carefully correlated with the pathologic changes. In this study we have found several varieties of pneumonia. (Examples were shown by lantern slide. The slides included clinical charts, roentgenograms, microscopic sections of whole lungs and photomicrographs.)

The chief forms of pneumonia found in this series were: (1) lobar (alveolar) pneumonia, (2) bronchopneumonia, (3) lobular pneumonia, (4) acute interstitial pneumonia and (5) septic pneumonia.

1. Lobar pneumonia is the variety seen most frequently clinically in New York City; it is seen less often at autopsy, because the mortality is low except in young infants and in cases complicated by meningitis or empyema. It appears at autopsy frequently enough, however, to make us certain that the disease occurs at all ages. It is almost the only form seen in persons more than 4 years of age. The clinical course in children is similar to that in adults, with defervescence by crisis, but the temperature often fluctuates more in infants. Bacteriologic studies show pneumococci of many types. The physical signs are those of local consolidation. The shadow appears in the roentgenograms very early, and is dense, massive and homogeneous. Pathologically, the lesion shows the characteristic alveolar exudate containing leukocytes, red cells and fibrin. The exudate is nearly uniform, although even in the consolidated lobes there may be a few air-containing lobules or occasional irregular patches. There is often a complicating purulent bronchitis, but the walls of the bronchi are not infiltrated with exudate. The interstitial framework of the lung is normal.

2. Bronchopneumonia occurs mostly in the first three years of life, in debilitated infants, after infectious diseases or intestinal intoxication, or as a terminal event in any fatal disease. The fever is usually less high than in lobar pneumonia; there is more real dyspnea; the course is long and irregular, and recovery is by slow lysis. The physical signs are often merely resonant râles at the bases of the lungs, or there may be areas of bronchial breathing. The lesion is in the wall of the bronchus, the outer coats of which are infiltrated with mononuclear cells resembling fibroblasts. These cells make a collar of varying thickness about the bronchus, often compressing the lumen in the severe cases. There is usually a purulent bronchitis, the lumen being filled with polymorphonuclear leukocytes. These may be seen migrating inward from the distended blood vessels; but there are practically no leukocytes in the area of mononuclear proliferation which begins immediately outside the region of the blood vessels and muscularis mucosae. There is often some consolidation in the alveoli near the bronchi, but this is mostly due to desquamation of epithelioid cells, with alveolar collapse, rather than to a true exudation. Confluence takes place by the extension of this process rather than by alveolar inflammation. There are often large areas of collapse, and the anterior borders of the lung are often emphysematous. Bronchogenic abscesses are found, and occasionally one of them ruptures into the pleural sac. This type of pneumonia casts no shadow in the roentgenogram taken in the early stages. Later there is a frayed-out appearance of the hilar shadow, with streaks running out into the pulmonary fields. Larger shadows are sometimes seen which are not very dense. These are due to areas of atelectasis. There is never a mottling of the lung with small round shadows. Streptococci are usually obtained on throat swab or in lung culture. Pneumococci are also often present, with or without streptococci. Staphylococci are found in the cases with bronchogenic abscesses.

3. Lobular pneumonia shows an entirely different lesion, and is best illustrated by the pneumonia due to the aspiration of sputum in newly born or feeble infants, or in persons with tracheo-esophageal fistula. It is seen in some cases of intestinal intoxication in which the presence of pneumonia has not been suspected. In other instances there is a long course with high, irregular fever resembling that of severe bronchopneumonia. The lesion is a patchy exudation confined to lobules scattered irregularly throughout the lung. There is nearly constant involvement of the lobules nearest the hilus, perhaps because the ventilation is least there. The exudate consists of polymorphonuclears and red cells, resembling that of lobar pneumonia, but is variable in different lobules, even those closely adjacent. This lesion is one which evidently invades the lobules by the lumen of the bronchus. The walls of the bronchi are not infiltrated, although there may be a purulent bronchitis. There is often confluence of the lobular lesions, whole lobes being solid, but there is much more variation in the lesions in different areas than in lobar pneumonia. The physical signs vary from those suggestive of bronchopneumonia (resonant râles only) to gross signs of massive consolidation. The roentgenogram shows a mottled, irregular shadow differing from that of bronchopneumonia and from that

of lobar pneumonia. The condition is usually diagnosed as tuberculosis from the roentgenogram. Bronchopneumonia and lobular pneumonia occasionally occur in the same lung, and it is probably this fact which has led so many writers to confuse them and to consider all cases of this type as representing varying forms of bronchopneumonia. The occurrence of each in pure form is so common, however, that it seems to us quite definite that when both are found the pneumonia must be considered as a mixed one.

4. Acute interstitial pneumonia is often called acute lymphangitis of the lung. It is characterized by a tremendous engorgement of the lymphatics of the lung, especially those in the septums separating the lobules and lobes. These are filled with closely packed leukocytes. There is edema of the fibrous tissue of the septums. The lung may look and feel solid, but this is due to collapse of the alveoli and edema. This type of lesion often complicates lobular pneumonia and sometimes bronchopneumonia.

5. In septic pneumonia there are found small septic infarcts with plugged vessels. There may be many or few.

It is worth while to separate the pneumonias of childhood into these types for several reasons. No excuse is needed to study any aspect of disease to find the real truth. But in pneumonia the prognosis varies so greatly in the different forms that the physician should know how to differentiate them. The great difference in roentgenographic shadows in cases in which there are signs of consolidation needs scientific explanation. It is only by correlating the clinical course and the roentgenographic shadows with the pathologic lesion that one can hope to arrive at an understanding of the disease.

WHY AND WHERE OUR BABIES DIE. DR. SHIRLEY W. WYNNE (Commissioner of Health, City of New York).

Looking back over the infant mortality rate prevailing in this city during the past generation, we are apt to point with pride to the great progress made in the prevention of infant mortality. Certainly few other public health activities have yielded such excellent results. In 1898, the year which marked the establishment of the greater city of New York, the rate was 141 per thousand births; this year it promises to be 50. Had the rate of 1898 prevailed in this city last year, 16,302 infants would have died during their first year. Actually only 6,427 died, so that nearly 10,000 lives were saved in a single year.

This is a very gratifying showing, but it must not delude us into believing that our work in this field is finished. Nor must we attribute too much to our public health efforts.

In the first place, consider the marked decrease in the birth rate. Taking only the reported number of births since 1898, there has been a reduction in the birth rate of from 24 to 16 per thousand. The actual reduction, however, is considerably greater than these figures indicate, because it is well known that the reporting of births was very incomplete in the earlier years. Careful calculations made in our bureau of records make it appear likely that the birth rate in 1898 was actually 36 per thousand, and that the registered number of births cannot be regarded as complete until about 1914. The true decrease in the birth rate is therefore from 36 to 16.

It has long been known that a decrease in the birth rate leads to a decrease in the infant mortality rate. The smaller number of children to be cared for by the mother permits and encourages better infant care. The marked decrease in the birth rate therefore discounts the reduction in the infant mortality rate as an achievement. We cannot credit all of the reduction to well organized health efforts. To be sure, largely through our effective control of the milk supply and through the educational work of the baby health stations, we have done a great deal to reduce the enormous number of deaths formerly occurring each summer as a result of diarrheal disease; we have also reduced the number of deaths due to tuberculosis and to some of the other communicable diseases. But little has been done to reduce the death rate during the first days of life.

During the three year period, 1929 to 1931, over one third of the infant deaths occurred during the first week of life, and over 50 per cent during the first month. It is clear that the activities ordinarily carried on by the department of health can have no effect on the more than 20 per cent dying on the first day. Can the department of health help to prevent any of the remaining deaths which occur within the first month? Let us examine the causes of death during this age period.

The deaths of infants in the first month of life are due largely to what are classed as "causes peculiar to the new-born." These are principally premature birth, injury at birth, atelectasis and various congenital malformations. Together they cause over 40 per cent of all infant deaths during the entire first year of life. We have, of course, no way to prevent congenital malformations, but these make up a relatively small proportion of the deaths charged to "causes peculiar to the new-born." By far the greater proportion is due to premature birth, injury at birth and atelectasis, and these would seem to be amenable to considerable reduction by better obstetrics.

Turning now to the deaths which occur after the first month of life (about 50 per cent of all infant deaths), our table shows that these are due mainly to infectious diseases, although a fair proportion is still charged to diarrheal disease. The pneumonias and bronchitis account for about half of the deaths charged to infectious diseases, and it is hard to see what preventive measures can be taken by the health authorities beyond still further education of parents regarding the communicability of respiratory diseases. The work of our baby health stations may result in a further reduction of deaths due to diarrheal disease, and the administrative control of the common infectious diseases of childhood may result in a decrease of the deaths now caused by these infections.

The making of Wassermann tests on expectant mothers as a routine and adequate prenatal supervision should also contribute to a reduction in the infant mortality rate. From what has been said, however, it will be clear that apart from certain "sore spots" in the city, which I shall discuss in a moment, the health department has about reached the end of its efforts to reduce infant mortality, and I do not see how the pediatrician can contribute very much more. The great loss of infant lives occurs before the pediatricians have charge of the infants in this city.

I feel strongly that the organized medical profession should face the facts brought out in this analysis and take steps to reduce what I consider to be still a considerable proportion of preventable deaths. Is the large number of deaths charged to injury at birth the result of too much operative interference with the normal course of labor? Does the high mortality charged to premature birth indicate insufficient prenatal care? Could not a considerable proportion of the deaths charged to atelectasis and asphyxia neonatorum be prevented by proper treatment? This and other questions which a study of the causes of death during and immediately following childbirth would suggest deserve careful study by the obstetricians. It seems to me that it would be desirable to refer this matter to a special committee, perhaps the same committee which is now studying maternal mortality. I feel confident that measures can be devised to reduce much of the high infant mortality now prevailing during and immediately after childbirth.

The health department ought also to contribute to the further reduction of infant mortality. It should concentrate its efforts on certain "sore spots," by which I mean areas in various parts of the city where the infant mortality rates are still far above the average for the borough in which the areas are located. Our recognition of these "sore spots" is the result of the analysis of our neighborhood health statistics.

For the past four years, we have been tabulating our vital statistics not merely on a city and borough basis, as was previously the case, but also on the basis of small geographic subdivisions which we call health areas. Moreover, we have subsequently combined the information for contiguous health areas into those for health center districts. For these subdivisions, that is, for health areas and

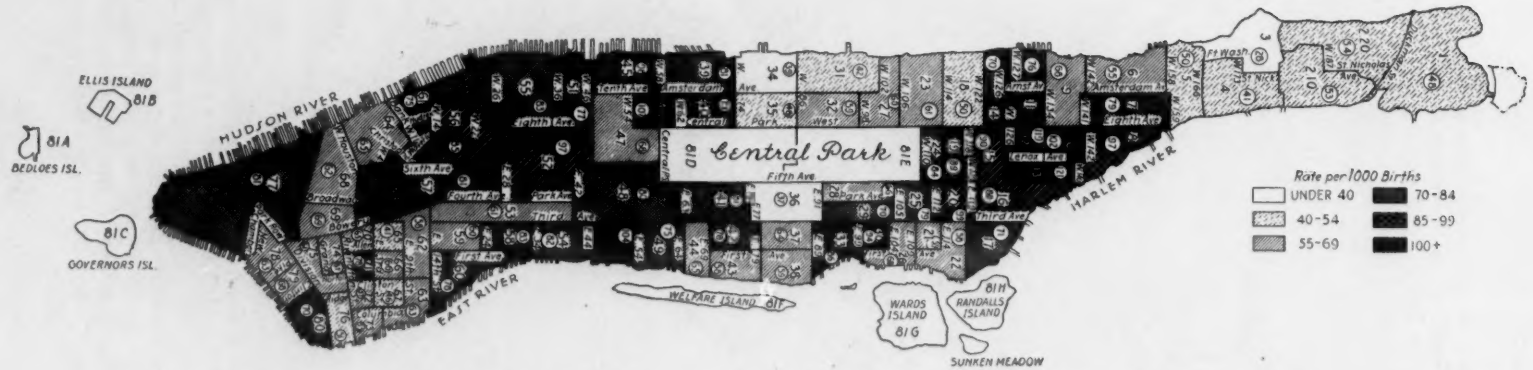

Chart 1.—Infant mortality rate by health areas, Manhattan, New York City, for the three-year period, 1929 to 1931. The figure inside of the circle refers to the annual average resident infant mortality rate per thousand live births. The figure outside of the circle refers to the health area. The data in this and the succeeding charts were compiled from health area statistics, Department of Health, City of New York, by the committee on neighborhood health development.

health center districts we now have valuable information regarding births and deaths, the latter being subdivided by age, sex and color and the more important causes of death. With population figures available through the Bureau of the Census we are able to express our figures in rates per hundred thousand and so make instructive comparisons between health conditions in various districts.

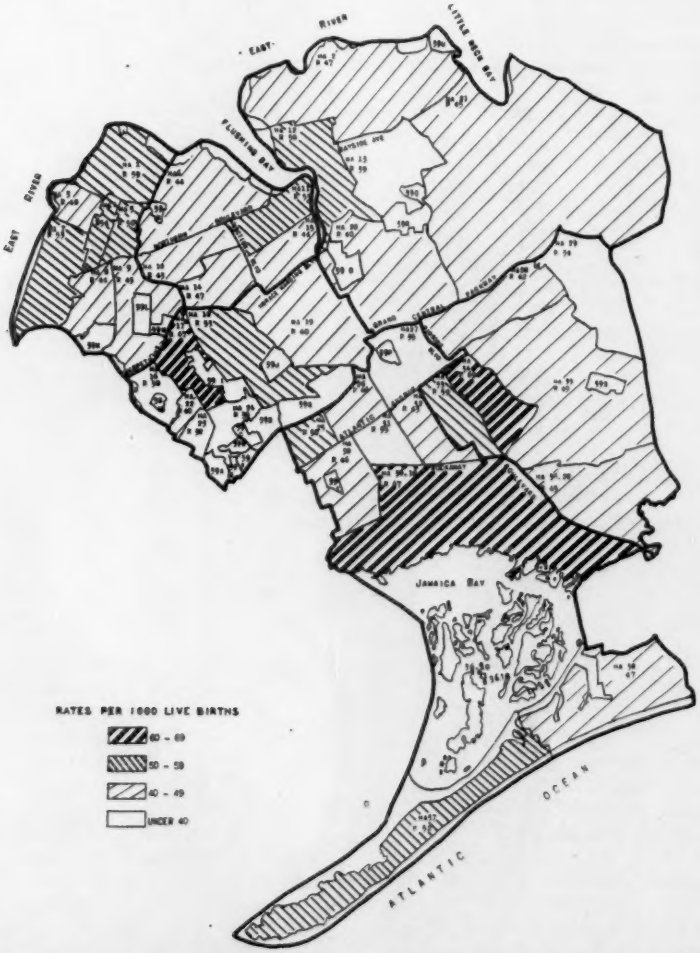

Chart 2.—Borough of Queens infant mortality rates by health areas for the three year period, 1929 to 1931. *HA* signifies health area; *R*, annual average rate; the heavy lines, the boundaries of the health center.

In the accompanying maps, I show the "sore spots" in the boroughs of Manhattan, the Bronx and Brooklyn. Let us look first at Manhattan.

Of the 7 health center districts into which the borough is divided, Central Harlem has the highest infant mortality rate, 97 per thousand births, as against 72 for the entire borough. The Lower West Side is next, with a rate of 80, and East Harlem is third, with 77. The other 4 districts have rates well below the borough average.

But our tabulations permit of a still further analysis, namely, by health areas, a health center district usually consisting of from 8 to 10 health areas. Whereas a health center district will usually have a population of about 250,000, a health area will include from 20,000 to 30,000 population. The health area is therefore comparable to a good-sized town, and when we utilize its statistics over a three year period, as we have done in our analysis, the figures are significant.

On the basis of health areas we find that in Manhattan there are 34 areas which have infant mortality rates above the borough average. Central Harlem has 2 areas in which the rates are very high, namely 121 and 119, respectively. Next after these comes an area on the Lower West Side which has a rate of 107, and

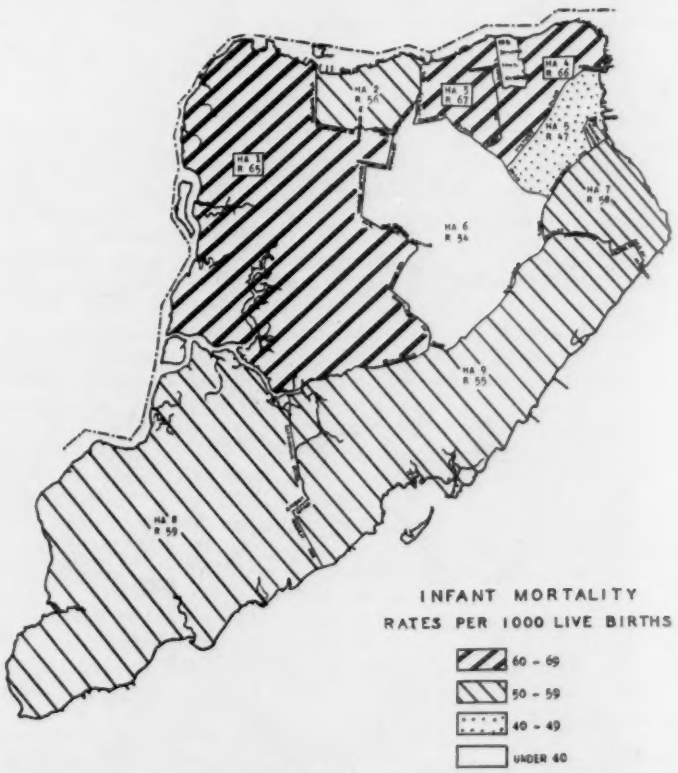

Chart 3.—Borough of Richmond infant mortality rates per thousand live births during the three year period, 1929 to 1931.

this is followed by one in Kips Bay-Lenox Hill district with a rate of 104. One more area with a rate over 100 is in Central Harlem.

The fact that most of the Manhattan areas with high infant mortality rates are in the Central Harlem Health Center District leads naturally to the question of infant mortality among Negroes. One of the areas with a very high rate, no. 46 in the Lower West Side district, has practically no Negro population. The high death rates among Negroes must not be regarded as a matter of higher susceptibility among Negroes as a race. A careful study of the problem indicates that fundamentally the problem is purely an economic one. Almost invariably the Negroes live in the poorer, more crowded, less sanitary sections of a city. In many instances, the wife as well as the husband is a wage earner. Under these circumstances,

it is clear that the infants do not receive the amount and kind of attention which they should have. Breast feeding is less common for the same reason. These factors, rather than any racial peculiarity, are mainly responsible for the high infant mortality among Negroes.

I do not want to take time to present the data in further detail, but I call your attention to the maps of the Bronx and Brooklyn in which the "sore spots" are shown in heavy shading.

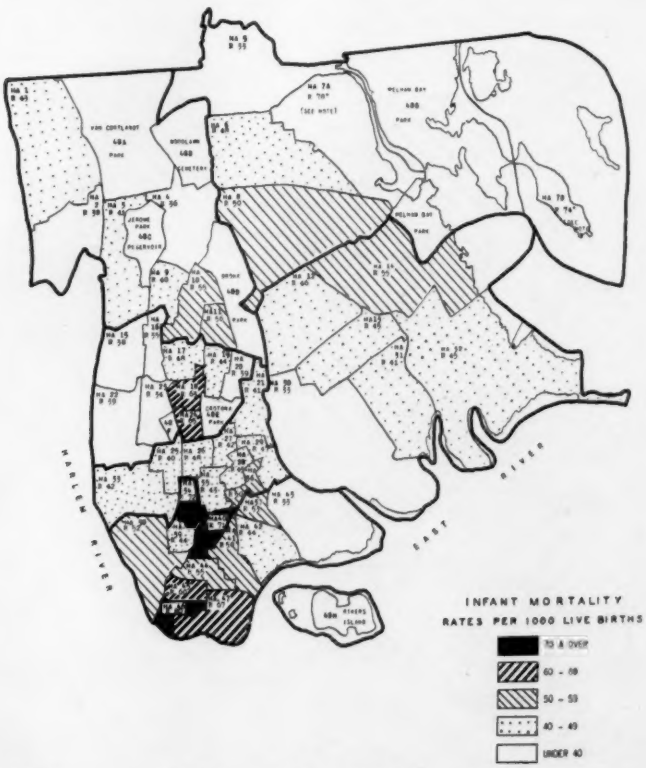

Chart 4.—Borough of the Bronx, infant mortality rates by health area for the three year period, 1929 to 1931. *Areas 7A and 7B with infant mortality over 70 per thousand births are not shaded black because the rates are based on only 3 and 5 deaths, respectively.

DISCUSSION

DR. PHILIP VAN INGEN: We are to be congratulated on having a commissioner of health come to the Academy of Medicine and ask us for help in making things better while saying so little about what he has done. We know what he is doing, and we ought to be very proud of his work.

We have heard some extremely interesting things tonight. Dr. Wynne has told us that the city's infant mortality rate for this year is likely to be around 50, and I think that he should admit that that is pretty good. I belong to that "last generation" he has mentioned, and remember that when the infant mortality rate in New York City first fell below 100 we felt that we had pretty nearly reached the limit. Now it is around 50, just half of that figure. Yet even today, the death rate of babies under a year of age is only surpassed by that of persons

at ages over 80. Please don't forget that. The baby today has no better chance of living a year than the man of 80. That is something to think about.

Dr. Wynne has called our attention to the fact that 50 per cent of the mortality of babies is during the first month of life. There has been something done; the medical profession is beginning to take a more active interest in neonatal mortality, that is, the mortality occurring during the first month of life.

The late Dr. Holt said years ago: "Babies in maternity wards are tolerated as one of the unavoidable incidents of obstetrical practice." Some of our obstetric friends take more interest in the babies than that, however. Many factors have brought this high mortality to the attention of the obstetrician.

Dr. Levy, in Newark, some years ago made a careful study of the mortality among babies according to who was present at the time of birth, and when a woman had been seen by a midwife during pregnancy, whether she presided at the birth or not, that baby's death was credited to the midwife. Dr. Levy showed that the figures were far from being flattering to physicians even when everything was taken into consideration. Obstetrics used to be largely a matter of watchful waiting. That is not the case today. The committee on obstetric care of the recent White House Conference brought out the fact that the responsibility for this was about fifty-fifty; the patients refused to wait and the physicians refused to wait. I think that it is the hurry that is often responsible. One thing that seems to bear this out is that—as you will find if you look at statistics throughout the country—deaths from accidents during labor have steadily been increasing since 1915. Dr. Wynne is right when he says something should be done about it. That is one of the places where we must make our attack.

I think that Dr. Wynne's statement regarding the importance of health districts is much to the point. In places where there are many poor who need these public health stations, there are none. They have been located largely according to density of population, and this is not the only basis.

There are a good many things we must consider, especially in these days when the city is not finding it easy to finance many of the things it ought to do.

Dr. Wynne has told us about health areas in the city. I fancy these health areas are practically little cities, little Hungarys, Austrias and Italys.

In that connection there are a number of things we might advantageously take into consideration. The statistics published by the Bureau of Vital Statistics of the federal government give some interesting facts in regard to the mortality of babies born in this country, according to the birth-place of the mother. Since the World War the immigration from Europe has been greatly diminished, and the effects of education on our foreign born have had a chance to be judged. In the five years from 1916 to 1920, the mortality among infants of foreign-born mothers in every national group except the Scandinavian (Norway, Sweden, Denmark) and the British (England, Scotland and Wales), was greater than that among babies of native-born mothers, and the difference was very marked in most cases, even as high as twice the rate. In the five year period from 1920 to 1925, in addition to the two groups mentioned, the Russian group had a lower rate of infant mortality than the native-born mothers; in the German, Irish and Italian groups the rates were almost the same as that for infants of native-born mothers. All showed a marked decrease. This is evidence of the effects of our widespread education.

But the statistics show more. They show that diarrheal diseases play a much greater part in the mortality among the infants of foreign-born mothers, especially those in the Polish, Austrian, Hungarian and, to a lesser degree, Italian groups. The same fact is true regarding respiratory diseases, the Italian babies dying almost as frequently as the Austrian, Hungarian and Polish. It would seem as if our attention should be directed toward combating these diseases in the areas where groups of these nationalities are concentrated.

And when we come to that neonatal mortality which Dr. Wynne has told us is responsible for over 50 per cent of the infant deaths, what do we find? The death rate of infants born to mothers of foreign birth, as a whole, is lower than

that of infants of mothers born in this country. Of the individual groups, Scandinavian, Russian and Italian mothers lose fewer of their babies than native-born mothers—the latter two foreign-born groups, almost 20 per cent less, while in the other groups the difference is only about 10 per cent more.

These facts, it seems to me, indicate the lines along which our energies in the various districts, these little Italys, Austrias, Hungarys and Irelands, may perhaps be best directed. They show, as Dr. Wynne has indicated, that among the mothers in all the groups, and perhaps particularly among those who are native-born, the problem of the neonatal mortality is a constant one and must be faced with renewed energy and perhaps new methods of approach. The fact that different racial groups present different problems of infant care after the first month of life suggests that our mode of attack may well be adapted to the special needs of each group, both in health department activities and in our own private and hospital work.

Pediatricians may well face these problems and, as in the past, render valuable service in solving them.

DR. BÉLA SCHICK: The tenor of the paper read by Dr. Wynne lies in his proposal to concentrate on infant welfare work conducted in these districts heavily shaded by infant mortality. This is a sound movement to be sure. The progress made in pediatrics in learning fundamental facts concerning the causes of morbidity and mortality in infancy, the application of this knowledge together with the continuous education of the public along these lines met with remarkable success in New York. The success is the more admirable as the size of the city and the continuous influx of less educated newcomers increase the difficulty of the situation. The situation is similar to that with tuberculosis. We cannot afford to interrupt this health education, and the department of health deserves high praise for its work. The infant mortality figures, however, can still be lowered. New Zealand is still the leading country in low infant mortality.

As I have said, I agree with the idea of somewhat decreasing the work in health education in those districts in which the population is more highly educated. The time, effort and money can be more advantageously used in the endangered districts of this city. But we have to consider that another problem in infant mortality exists which was brought out in the statistics given tonight. This problem is the "early mortality of infants," that is, the mortality of infants during the first week of life. There are high figures, especially for the first three days of life. We pediatricians feel that this part of infant mortality deserves our undivided attention. The figures for the mortality of infants who have survived the first eight days of life are approaching the possible minimum. It is calculated that a mortality of about 4 per cent is inevitable, principally on account of respiratory diseases. Much more room for improvement lies in the period of early infancy covering the first week of life. Intensive efforts should be expended in the study of this problem. It is intimately connected with obstetric problems, and I am convinced that only the cooperation of the obstetrician with the pediatrician will bring about progress in this respect.

It would lead too far afield to discuss the problem of the mortality in early infancy. I wish only to point out that in spite of the falling birth rate and the falling rate of the mortality in later infancy, the mortality in early infancy and the number of stillbirths are increasing. These facts are mainly explained by three factors: (1) the increase in the percentage of children who are first born; for instance in 1901, among 100 legitimate children born in Berlin, 30 were first born, while in 1926 among 100 legitimate children born in Berlin 49 were first born; (2) the increase of the age of mothers giving birth to a first child with greater risk for the delivery, and (3) the greater tendency of older mothers with a first pregnancy to deliver the child prematurely, and the greater susceptibility of these premature children to birth injury.

In conclusion, I wish to make a plea for a concerted attack on the problem of mortality in early infancy by obstetricians and pediatricians. The mother who

goes through the hardship of a nine months' pregnancy has a right to expect that science and the community should do everything to save the life and health of the child when born.

DR. HERBERT B. WILCOX: Dr. Wynne's problem seems well nigh insolvable because of its complexity and size.

The city has doubled its population in the past thirty-four years, and even the present method of subdivision leaves these areas so large as to make successful health administration difficult. For statistical purposes great advantage accrues from this subdivision, but in the matter of control of disease the results are of necessity less definite, because the population of these "sore spots" is not confined within the limits of the subdivision but roves, tending to spread whatever infection is present in the district.

From what has been said this evening, it would seem that this meeting might well have been held under the auspices of the section on obstetrics and gynecology, as infant mortality in the past years has steadily represented largely conditions pertaining to the early postnatal period, rather than to the latter months of infancy.

We are all interested in the increase of life expectation for the newly born child. There is, however, something of the old habit of survival of the fittest in the secondary consideration given the child by the obstetrician as compared with the attitude of the pediatrician of making those less fit ones more fit.

The effort at correction should be primarily aimed at the prenatal, natal and neonatal periods. Diseases peculiar to the new-born may, at least to a certain extent, be placed in the preventable class. They are responsible for a total of about 40 per cent of all infant deaths. Of these neonatal conditions, congenital malformations contribute about 18 per cent of the deaths. These may or may not be amenable to correction. Prematurity causes about 54 per cent. Certainly much can be done to control this cause of death. Birth injuries are responsible for about 12 per cent. It is fair to assume that many of these are avoidable. Atelectasis furnishes about 11 per cent, and this too should be amenable to control in some degree.

Prematurity, birth injuries and atelectasis are responsible for about 77 per cent of the diseases peculiar to the new-born now classed as nonpreventable. Steps toward improvement of prenatal care, maternal health education, obstetric care and improvement of home conditions to which these new-born children return, may well be expected to show a favorable influence on these causes of early mortality.

One condition in particularlar stands out as certainly amenable to correction. Under the present system, expectant mothers are actually discouraged from applying for prenatal registration in private hospitals because, if they do so, confinement care in city institutions is available to them only as an emergency service. This means that obstetric care is always too late, for the term "emergency" implies active labor. These expectant mothers are inclined to register for prenatal care at private institutions because the city clinics are overcrowded and not as well run as they should be. The same is true of the city obstetric services, as is proved by the large amount of gynecologic work found necessary in them, probably an illustration of hurried or inadequate obstetric aid. Here is one definite chance for a reduction in some of the causes of early mortality.

Next to this comes the hiatus which exists between obstetric and pediatric care. An attempt has been made to meet this requirement by the establishment of the baby health stations but, manned as they of necessity must be, the best pediatric advice is not available.

Among the things necessary for the correction of some of these factors should be: (1) doing away with the system which discourages women from getting advice and care during the prenatal period; (2) provision of better and longer maternal care at the time of confinement; (3) a combination of the baby health stations with well established pediatric outpatient departments; (4) a combination of health department nursing and hospital social service, and (5) more effort in the neonatal period—if necessary, at the expense of the effort now put into school medical inspection.

DR. LOUIS C. SCHROEDER: Dr. Wynne's paper is a challenge to pediatricians. We can do nothing less than accept it in full, and if this study passes into the limbo of forgotten things it will be a misfortune. This challenge has already been discussed in full by three able men, one of whom in particular, Dr. Van Ingen, has kept in as close touch with infant mortality statistics as any one. It will perhaps be best if at the end of this meeting we emphasize the main points which have been made so that this particular problem can be seen wholly and clearly.

The solution of the problem of infant mortality is not finished. It follows logically that all pediatric groups should arrange at least once a year to discuss and act on it.

A number of conditions which cause death among the new-born have shown no reduction during the past generation, and Dr. Wynne feels that these should engage the attention of all obstetricians. There is one condition in this group which is in need of revaluation. That is "birth injury." Granted that poor obstetrics may produce injuries of the brain, it does not follow that every child in whom there is hemorrhage into the brain has been handled badly. The closer the situation is studied, the more apparent it becomes that hemorrhages found in the new-born at autopsies may be due to a number of causes, some of them in no way related to the obstetric procedures which have been employed.

This leads naturally to the conclusion that more detailed studies cannot possibly be conducted properly by either the obstetrician or the pediatrician alone. Each must contribute a part. It is decidedly a problem for cooperative effort, calling as it does for both antenatal and postnatal data.

Dr. Wynne's citation of the toll of death from infectious diseases after the first month once more emphasizes the need of educating parents to the necessity of keeping their infants away from persons who have colds.

The most vivid and probably the most valuable part of the essay has been that directing attention to the "sore spots" in the city. The location of a target is certainly the most important part of effective firing, and while most every one knows that certain areas have higher death rates than others it scarcely seems possible that in Manhattan there is as wide a variation as exists between the rate of 28 in Washington Heights and that of 121 in Central Harlem.

Dr. Wynne's plea for help from organized medicine cannot go unheeded.

DR. SHIRLEY WYNNE: Dr. Wilcox mentioned school medical inspection and suggested cutting the budget for that service and devoting more funds to work among infants. This matter is now under consideration by a committee of which Dr. Van Ingen is chairman. When his committee reports, we will be able to decide whether or not the school medical work is paying sufficient dividends or whether the money should be diverted to some other activity. It is possible that we may eliminate it entirely. In the last three years, we have doubled the number of examinations, and they have been made better, without increasing the budget.

The association of our health centers with hospitals and universities would be welcomed by the department. As we asked the universities to take an active interest in diphtheria prevention, we have asked them also to take an active interest in the work of our baby health stations. It would be well if the medical schools could arrange to have some of their men on the staff of these stations permanently.

One of those who took part in the discussion pointed out that the hospitals which maintain maternity services and receive payment from the city for the care of emergency cases cannot or will not give prenatal care because by doing so they are unable to meet the terms of the law which entitles them to payment for the care of city charges. We all appreciate the importance and indeed the necessity of prenatal care, and I am sure that if the matter were properly presented to the mayor and the board of estimate they would see the advantage of prenatal service.

As I understand it, the law specifically provides that the city may pay private hospitals only for the care of emergency cases, and I imagine that this law will have to be amended in order to permit the giving of prenatal care to city charges.

The members of your section are always helpful, and I appreciate the value of the contribution they have made to our work.

Book Reviews

Lectures on Midwifery and Infant Care. By T. F. Corkill, M.D., M.R.P. (Ed.). Price, 12s, 6d. Pp. 419. Wellington, New Zealand: Coulls Somervill Wilkie, Ltd., 1932.

This book was written primarily for nurses and midwives. The detail with which certain problems of the management of labor and medical therapeutics are described suggests that nurses in New Zealand are permitted to execute measures the performance of which by them, at least in this country, would seem to be intolerable. The acknowledgment by the author that "many of our nurses are already generally trained, and, having a high standard of knowledge, enquire full information" does not seem to justify such an attitude. This criticism must be reversed if the book is to be used, as the author hopes, by medical students and physicians. For this group there is insufficient detail, especially in respect to treatment.

The text is in outline form. Throughout there runs a preventive trend that is admirable. In some instances even more emphasis would be valuable. Nursing technic has been well standardized. The danger of the use of pituitary extract in the first and second stages of labor is stressed. Under puerperal care, the remark ". . . but it is a mistake to ply the woman with excess of sloppy foods," is apt, as is the term "so-called galactogogues."

The value of diet and of the use of dextrose in the treatment of the toxemias of pregnancy is skimped or not mentioned, while that of the more or less questionable use of alkalis is overemphasized. Trichomonas vaginalis is not mentioned.

The paragraph dealing with "when the nurse should send for the doctor" would, no doubt, meet with the approval of most physicians, but would not be conducive to reduction of the infant mortality rate, for proper medical attention is as important during labor as it is during delivery. No mention is made of the determination of the fetal heart rate during the second stage. In the chapter on asepsis, Lister and Pasteur are mentioned, but the work of Semmelweiss is ignored.

The short portion of the book devoted to the new-born is instructive. The prophylaxis of pemphigus neonatorum and the treatment of thrush (gentian violet) are not mentioned. The chapters on asphyxia, intracranial hemorrhage and prematurity are well written.

The four hour feeding interval with omission of night feeding is advocated, and the importance of breast feeding is sufficiently emphasized. The exposition of the percentage method of feeding is of reminiscent interest to the reviewer, who dispensed with the science of mathematics when this system was abandoned. This method is advocated by the Plunket Society of New Zealand, which has devised a system of infant care and instruction to mothers. It is interesting to read of the development of several formulas for humanized milk in which butter fat is largely replaced by emulsions of various fats and oils, partly animal and partly vegetable, much as has been done in this country by certain commercial concerns.

While this book is probably not adaptable for use in America, it undoubtedly serves an excellent purpose in the country of its origin.

Die Tuberkulose. By W. Schmid-Sachsenstamm and Carl Waitz. Price, 10 marks. Pp. 230, with 46 illustrations. Vienna: Franz Deuticke, 1933.

This inexpensive volume portrays the modern conception of the various forms of tuberculosis in a concise and practical manner. Brief introductory discussions of the tubercle bacillus and methods and routes of human infection with this organism are followed by more comprehensive considerations of the pathogenesis and

pathology of tuberculosis, not only of the primary complex, but also of post-primary, intrapulmonary and extrapulmonary stages of the disease. The clinical features, diagnosis and methods of treatment of various types of tuberculosis as seen in infants, children and adults are ably discussed in a conservative manner.

Other topics that are treated in the text include the reaction to tuberculin and tuberculo-immunity, pregnancy and tuberculosis and the nontuberculous conditions which must be considered in differential diagnosis. Forty-six illustrations are shown, of which thirty-eight are reproductions of x-ray films, portraying various forms of pulmonary tuberculosis particularly.

An instructive and ingenious schematic representation of the evolution of tuberculosis in the human body directly and indirectly from the primary focus is appended. The volume contains no references to the literature, hence it is not suitable for use as a reference text. It was prepared by the authors as a guide for practitioners of medicine, and for this purpose it is exceedingly satisfactory.

Sex and Internal Secretions. By Edgar Allen and collaborators. Price, $10. Pp. 951, with numerous charts, illustrations and tables. Baltimore: Williams & Wilkins Company, 1932.

This large and rather closely printed volume represents a "stock-taking" of the work done under the stimulus of the Bureau of Social Hygiene with the administrative guidance of the Division of Medical Sciences, of the National Research Council, and covers the accomplishments since November, 1921.

The work is a compilation contributed to by twenty-three well known and competent men in the fields of physiology, biology, medicine and endocrinology. A complete review of so exhaustive a volume is obviously impossible. Its chapters deal with general biologic and hereditary considerations; the interrelations of genetic and endocrine sex factors; the embryologic development of sex factors; sex deviations, inversions and parabiosis; the physiology of sex; the biology, physiology and chemistry of the sex glands and their secretions; an excellent résumé of the research on plumage tests in birds; the physiology of insemination and fertilization; the effect of other endocrine secretions on the gonads and secondary sex characteristics; the sexual drive, and a summary of endocrine disorders of sex function in man.

The reaction of the reviewer after reading this painstaking and complete work was a hearty desire to see a similar project consummated in the general field of endocrinology. Such works are of inestimable value as reference works for the practitioner of medicine. Dr. Allen and his collaborators are to be congratulated on the production of an extremely interesting and authoritative book.

The Expectant Mother's Handbook. By Frederick C. Irving, M.D. Price, $1.75. Pp. 203. Boston: Houghton Mifflin Company, 1932.

"The Expectant Mother's Handbook" by Frederick C. Irving is unquestionably one of the best books of its type in print today. It presupposes no knowledge of medical subjects by the patient and answers clearly all questions which are commonly asked of the physician. The facts are stated in scientific terms, which in turn are clearly defined in such a manner that the laity can without difficulty understand the different topics which the author discusses. He takes up the organs of reproduction, conception, methods of diagnosis of pregnancy, growth of the fetus, general hygiene, minor and major complications and their allied subjects. The reading of this book by the expectant mother will give her a clear idea as to the physiology of her pregnancy and save the physicians many hours of explanation of the questions most frequently asked by the average woman.

Child Psychology. By Buford J. Johnson. Price, $4. Pp. 439, with 50 figures and plates. Springfield, Ill.: Charles C. Thomas.

This book covers the usually discussed phases of normal mental development in children. More than most books it attempts to combine physiologic psychology

with every-day problems. There are chapters on learning, attention, perception and thought on the one hand, and a consideration of infant response, social behavior and personality on the other. Countless illustrations of every-day problems met with in children make the reading of the report interesting. A discussion of each subject includes a review of the literature followed by the author's point of view.

As a whole, the discussions are academic in character. The point of view is of the physiologic psychologist or educator. Psychiatric views and problems are not included.

The book is well written, and the material is presented in an interesting manner. It should be of interest to parents and teachers.

Calcium Metabolism and Calcium Therapy. By Dr. Abraham Cantarow. Second edition. Price, $2.50. Pp. 252. Philadelphia: Lea & Febiger, 1933.

In this book the author applies the physiologic and biochemical developments in calcium metabolism to practical clinical use. The experimental and laboratory findings in both normal and abnormal calcium metabolism are employed as a foundation on which rational calcium therapy in pathologic conditions is based. The literature on this subject has been thoroughly consulted, and the essential principles and opinions are concisely presented. All diseases in which calcium metabolism plays a rôle are considered in detail from both the purely scientific and the clinical point of view. Changes in the second edition of this volume include the relationship between the parathyroid hormone and vitamin D, the significance of phosphatases in the mechanism of ossification and in diseases of the bone, dental caries, the influence of calcium on the pharmacologic action of various drugs and the nature of the action of the parathyroid hormone.

Hygiene des Fusses. By Prof. Dr. F. Schede. Price, 1.50 marks. Pp. 42. Leipzig: Georg Thieme, 1932.

This work directs the physician's attention to the feet of children and adults, emphasizing the importance of treating the whole patient and not merely the condition of the feet.

The author traces the formation of flatfoot from its origin in childhood to the vicious circle present in the adult, outlining the steps necessary in prevention and cure once the condition is established. The scope of the work ends where orthopedic intervention is indicated. Exercises are given.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Secretary: Dr. Leonard K. Findlay, 61 Harley St., London, W. 1.
Place: London. Time: July 20-23, 1933.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.
Place: London. Time: May 26, 1933.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: June 12-16, 1933.

American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

American Pediatric Society

President: Dr. Oscar M. Schloss, 1185 Park Ave., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Washington, D. C. Time: May 8-10, 1933.

Canadian Society for the Study of Diseases of Children

President: Dr. Frederick F. Tisdall, 170 St. George St., Toronto, Ontario.
Secretary-Treasurer: Dr. T. G. H. Drake, 67 College St., Toronto, Ontario.

Society of Pediatric Research

President: Dr. Bengt Hamilton, University of Chicago, Chicago.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston
Place: New York. Time: May 6, 1933.

SECTIONAL

Central States Pediatric Society

President: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Chicago. Time: Sept. 22-23, 1933.

North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Richmond, Va. Time: November, 1933.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. M. Hines Roberts, Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, 3503 Prytania St., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 6th St., Tulsa.

South Carolina Pediatric Society

President: Dr. J. I. Waring, 77 Rutledge Ave., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, Medical Bldg., Florence.

Texas Pediatric Society

President: Dr. Boyd Reading, 2201 Avenue D, Galveston.
Secretary-Treasurer: Dr. F. W. Hoehn, 1006 Medical Arts Bldg., Waco.

Virginia Pediatric Society

President: Dr. J. B. Stone, 2042 Park Ave., Richmond.
Secretary-Treasurer: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. George M. Lyon, 955, 4th Ave., Huntington.
Secretary: Dr. M. F. Petersen, 1013 Quarrier St., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. C. W. Burhans, 14805 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. J. A. Garvin, 2009 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Edward L. Benjamin, 2021 Grand Concourse, New York.
Secretary: Dr. Harry M. Schapiro, 1882 Grand Concourse.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Every Second Wednesday of each month, except June, July, August and September. Annual meeting, May 10, 1933.

Brooklyn Pediatric Society

President: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Archibald L. Hoyne, 25 E. Washington St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Bernard Bernbaum, 5057 Woodward Ave., Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

International Pediatric Society

President: Dr. Barnet E. Bonar, 9 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Memphis Pediatric Society

President: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. D. Mims, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Karl E. Kassowitz, 709 N. 11th St., Milwaukee.
Secretary: Dr. John H. Reynolds, 747 N. 27th St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Thomas A. Foster, 131 State St., Portland, Maine.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. John Caffey, 50 Haven Ave., New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Irving McQuarrie, Dept. Pediatrics, University of Minnesota, Minneapolis.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelphia Pediatric Society

President: Dr. Joseph Stokes, 159 W. Coulter St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. F. Waring Lewis, Professional Bldg., Richmond, Va.
Secretary-Treasurer: Dr. A. S. Hurt, Jr., 2618 Grove Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Albert S. McCown, 509 Olive St., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Gustave F. Weinfeld, Moraine Hotel, Highland Park, Ill.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1933.